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SPRING COLLEGES IN COMPUTATIONAL PHYSICS

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MOLECULAR DYNAMICS
I-II-III

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MOLECULAR DYNAMICS SIMULATION

OF (COMPLEX) MOLECULAR SYSTEMS

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- YET ANOTHER (BRIEF) INTRODUCTION TO MD
- TIPS FOR MOLECULAR SYSTEMS
  - CONSTRAINT DYNAMICS
  - LONG RANGE FORCES
  - MULTIPLE TIME STEPS (REVERSIBLE ALGORITHM
- BEYOND MICROCANONICAL MD : EXTENDED SYSTEMS
  - NOSÉ'S CONSTANT TEMPERATURE
  - ANDERSEN'S CONSTANT PRESSURE

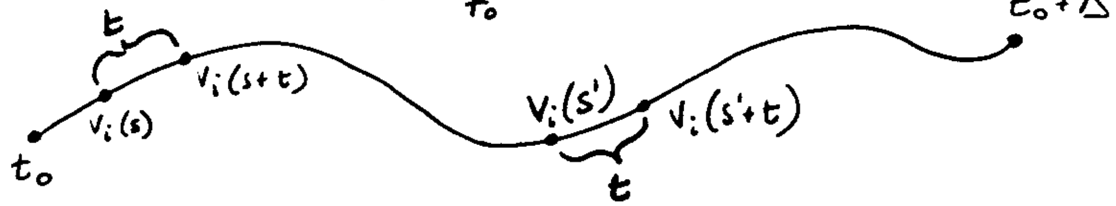
TIME CORRELATION FUNCTIONS

$$D = \frac{1}{3} \int_0^\infty dt \; < \vec{V}(t).\vec{V}(0) >$$

$\vec{V}_i(t)$ VELOCITY OF PARTICLE i AT TIME t

$$< \vec{V}(t).\vec{V}(0) > = \frac{1}{N} \sum_{i=1}^{N} < \vec{v}_i(t).\vec{v}_i(0) >_\Delta$$

$$< V_i(t).V_i(0) >_\Delta = \frac{1}{(\Delta)^*} \int_{t_0}^{(t_0+\Delta)^*} ds \; V_i(s+t).V_i(s)$$



AVERAGE OVER PAIRS SEPARATED BY AN INTERVAL t

SHEAR VISCOSITY $\eta = (V k_B T)^{-1} \int_0^\infty dt < \sigma^{xy}(0)\, \sigma^{xy}(t) >$

$$\sigma^{xy} = \sum_{i=1}^{N} p_i^x p_i^y / m_i + \frac{1}{2} \sum x_{ij} f^y(r_{ij})$$

THERMAL CONDUCTIVITY $\lambda_T = (V k_B T^2)^{-1} \int_0^\infty dt < J_z^e(t)\, J_z^e(0) >$

$$J_z^e = \frac{d}{dt} \left(\sum_{i=1}^{N} z_i \frac{1}{2} \left(p_i^2/m_i + \sum_{j \neq i} u(r_{ij}) \right) \right)$$

DYNAMICAL STRUCTURE FACTOR

$$S(\vec{k},\omega) = \text{F.T.} \left[\frac{1}{N} < \rho(\vec{k},t)\, \rho(-\vec{k},0) > \right]$$

$$\rho(\vec{k},t) = \sum_{i=1}^{N} b_i \, e^{i \vec{k}.\vec{r}_i(t)}$$

- EQUIPARTITION OF ENERGY ⇒ TEMPERATURE ESTIMATOR

$$\mathcal{T}(t) = \frac{1}{3Nk_B} \sum_{i=1}^{N} \vec{p}_i^{\,2}/m_i \qquad \text{[PHASE FUNCTION]}$$

TEMPERATURE $$T = \lim_{\Delta \to \infty} \frac{1}{\Delta} \int_{t_0}^{t_0+\Delta} dt \; \mathcal{T}(\Gamma(t))$$

- VIRIAL THEOREM → PRESSURE ESTIMATOR

$$\mathcal{P}(t) = \frac{Nk_B\mathcal{T}(t)}{V} + \frac{1}{3V}\sum_{i=1}^{N} (\vec{r}_i \cdot \vec{f}_i) \qquad \text{[P.F.]}$$

PRESSURE $$P = \lim_{\Delta \to \infty} \frac{1}{\Delta} \int_{t_0}^{t_0+\Delta} dt \; \mathcal{P}(\Gamma(t))$$

- OTHER RELATIONS FROM FLUCTUATIONS...

  heat capacity at CONSTANT VOLUME C_V

$$\langle (K.E.)^2 \rangle_{NVE} - \langle K.E. \rangle_{NVE}^2 = \frac{3k_B^2 T^2}{2N}\left(1 - \frac{3k_B}{2C_V}\right)$$

- ENTROPY AND FREE ENERGIES ...

  ... FROM THERMODYNAMIC INTEGRATION...

  AND OTHER METHODS (SAME AS MONTE CARLO...)

AND LAST BUT (CERTAINLY) NOT LEAST

- DYNAMICAL PROPERTIES
  - ○ SELF DIFFUSION COEFFICIENTS } SINGLE PARTICLE
  - ○ RELAXATION TIMES
  - ○ VISCOSITY } COLLECTIVE
  - ○ THERMAL CONDUCTIVITY
  - ○ RATE CONSTANTS

... FROM TIME DEPENDENT CORRELATION FUNCTIONS

THE IDEA: SIMULATE A REAL EXPERIMENT

- SAMPLE PREPARATION:
  - CHOICE OF A MODEL SYSTEM (Potential - BOUNDARY-C
    i.e. of $\mathcal{H}$ AND THERMODYNAMICS CONDITIONS (N.V.E.
  - INITIAL CONFIGURATION (POSITIONS & MOMENTA)

- PERMORMING THE MEASUREMENT
  - SOLVE NEWTON'S EQUATIONS OF MOTION (NUMERICA ALGORITHM
  - CONTROL EXPERIMENTAL CONDITIONS (P, T, ...)
  - RECORD ALL POSSIBLE PHYSICAL PROPERTIES.
    (FULL PHASE SPACE TRAJECTORY)

- ANALYZE MEASURED RESULTS.
  - STATISTICS, PLOTTING, ...

- RESULT OF AN MD SIMULATION IS A PHASE SPACE TRAJECTORY OF THE SYSTEM UNDER STUDY FROM TIME t_0 TO TIME $t_0 + \Delta$

OBSERVABLE $A(\{\vec{r}, \vec{p}\}) \equiv A(\Gamma)$

TIME AVERAGE

$$\langle A \rangle_\Delta = \frac{1}{\Delta} \int_{t_0}^{t_0+\Delta} dt \, A(\Gamma(t))$$

FOR ERGODIC SYSTEMS IN THE LIMIT OF LARGE Δ

$$\lim_{\Delta \to \infty} \langle A \rangle_\Delta = \underbrace{\int d\Gamma \, \rho(\Gamma) \, A(\Gamma) = \langle A \rangle}_{\text{ENSEMBLE AVERAGE}}$$

MD → MICROCANONICAL ENSEMBLE $\rho \propto \delta(\mathcal{H} - E)$

$$\mathcal{H} = K + \mathcal{V}$$

KINETIC ENERGY $K = \sum_{i=1}^{N} \vec{p}_i^{\,2}/2m_i$

POTENTIAL ENERGY $\mathcal{V} = \mathcal{V}(\vec{r}_1, \vec{r}_2, \ldots, \vec{r}_N)$

EQUATIONS OF MOTION

$$\dot{\vec{r}}_i = \frac{\partial \mathcal{H}}{\partial \vec{p}_i} \qquad \dot{\vec{p}}_i = -\frac{\partial \mathcal{H}}{\partial \vec{r}_i}$$

GIVEN THE INITIAL CONDITION $\{\vec{r}_1(t_0), \ldots, \vec{p}_1(t_0) \ldots\}$

NUMERICAL SOLUTION

- δt DISCRETE TIME STEP
- ALGORITHM
  - ACCURACY
  - COMPUTATIONAL COST (MEMORY & CPU TIME REQ.)
  - STABILITY

MOST POPULAR: VERLET ALGORITHM (VELOCITY VERSION)

START FROM A REGULAR TAYLOR EXPANSION UP TO 2nd ORDER in δt

$$\boxed{\vec{r}_i(t+\delta t) = r_i(t) + \delta t\, \vec{v}_i(t) + \frac{\delta t^2}{2m_i} \vec{f}_i(t)}$$

AND TIME REVERSED TAYLOR EXPANSION

$$\vec{r}_i(t) = \vec{r}_i(t+\delta t) - \delta t\, \vec{v}_i(t+\delta t) + \frac{\delta t^2}{2m_i} \vec{f}_i(t+\delta t)$$

OBTAIN FOR VELOCITIES

$$\boxed{\vec{v}_i(t+\delta t) = \vec{v}_i(t) + \frac{\delta t}{2m}\left[\vec{f}_i(t) + \vec{f}_i(t+\delta t)\right]}$$

[KEEPS TIME REVERSAL PROPERTY OF THE E. of M.]

- COMPLETELY EQUIVALENT TO VERLET (IDENTICAL TRAJECTORIE
- VELOCITIES ARE ONE STEP BEHIND

  NEEDS $\vec{r}_i(t+\delta t) \rightarrow \vec{f}_i(t+\delta t)$ TO EVALUATE $\vec{v}_i(t+\delta t)$
- INITIAL CONDITION IN TERMS OF $\{r_i\}$ & $\{v_i\}$ at same TIME t_0.

- ONLY ONE FORCE EVALUATION PER STEP
- STABILITY FROM TIME REVERSAL PROPERTY
- SHORT TIME ACCURACY IS NOT VERY HIGH $O(\delta t^3)$

  $\longrightarrow$ SHORT TIME STEP δt
- GOOD LONG TERM ENERGY CONSERVATION

  $\longrightarrow$ NO LONG TERM ENERGY DRIFT PROBLEM

HARDLY HELP TO USE A BETTER ALGORITHM

EXPONENTIAL GROWTH OF THE ERROR IN THE TRAJECTORY

MD TRAJECTORY CLOSE TO TRUE TRAJECTORY
ONLY FOR A FEW HUNDRED TIME STEP
SO CALLED : LYAPUNOV INSTABILITY

CONSIDER TWO SLIGTHLY
DIFFERENT INITIAL CONDITIONS

$$\Gamma_0 = \{r_i(t_0)\};\{p_i(t_0)\}$$

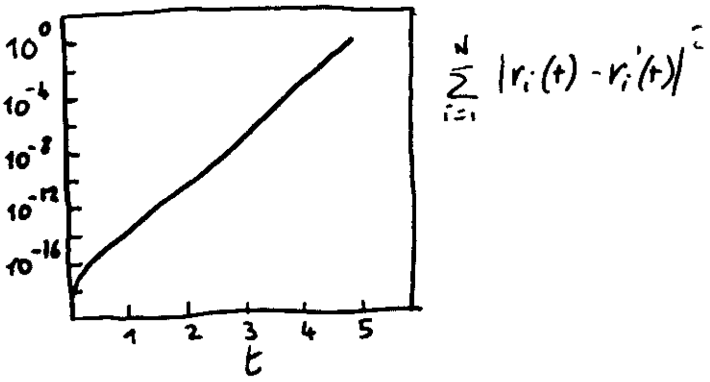
$$\Gamma_0' = \{r_i(t_0)\};\}p_i(t_0)+\varepsilon\}$$

$$r(t) = f(\Gamma_0; t)$$

$$r'(t) = f(\Gamma_0'; t)$$

$$|\Delta r(t)| \sim \varepsilon\, e^{\lambda t}$$

λ LARGEST LYAPUNOV EXPONENT



1000 STEPS $\delta t = 0.005$

IT HELPS STATISTICAL AVERAGES !

LONG TRAJECTORY $\Rightarrow$ MANY UNCORRELATED INITIAL CONDITIONS

CHOICE OF MODEL

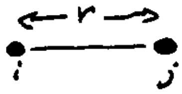
$$V = V_{BO}(\vec{r}_1, \vec{r}_2, \dots \vec{r}_N)$$ BORN OPPENHEIMER

[EFFECTIVE POTENTIAL - PAIR INTERACTIONS]

- MODELLING V_{BO}
  - BONDED INTERACTIONS (ATOMS CONNECTED BY CHEMICAL BONDS)
  - NON-BONDED INTERACTIONS (ATOMS IN DIFFERENT MOLECULES OR ...)

BONDED INTERACTIONS

- BOND STRETCHING (2 atoms)



$$V_{bond}(\vec{r}_{ij}) = \frac{k_b}{2}(r_{ij} - b_0)^2$$

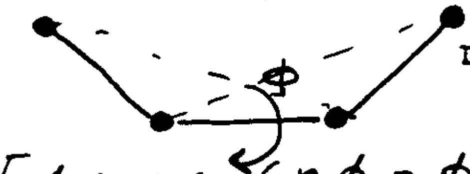
ij - bonded pair

- BOND BENDING (3 atoms)

$$V_{BEND}(\vec{r}_{ij}, \vec{r}_{ik}) = \frac{k_\theta}{2}(\theta_{ijk} - \theta_0)^2$$

i j k - bonded tern

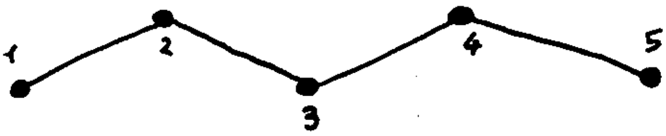
- TORSION (4 atoms)



DIHEDRAL ANGLE

$$V_{TORSION}(\phi) = V_\phi[1 + \cos(n\phi - \phi_0)]$$

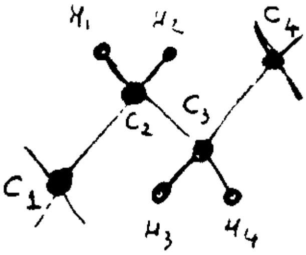
- 1-4 INTERACTIONS (2 atoms)



PAIR INTERACTION BETWEEN ATOMS FAR APART IN THE CHAIN, i.e. 1-4, 1-5, ...

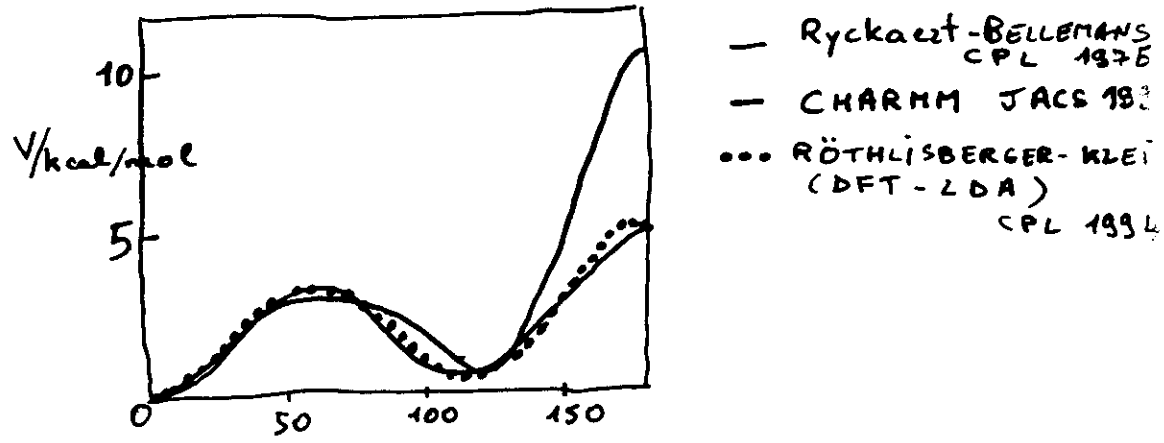
USUALLY IDENTICAL TO NON BONDED INTERACTION (Lennard-Jones + Coulombic) BUT MULTIPLIED BY A SCALE FACTOR.

(• CONSTRAINTS ...)



CHARACTERISTIC FREQUENCIES (cm^{-1})

STRETCHING	C-H	2900
	C C	960
BENDING	H-C-H	906
	C-C-H	760
	C-C-C	490
TORSION	C-C-C-C	145



NON BONDED INTERACTIONS

- HARD CORE REPULSION (SHORT RANGE)

$$V_R(\vec{r}_{ij}) = A_{ij} \exp(-B_{ij} r_{ij})$$

or $A_{ij}\, r_{ij}^{-n}$ (usually $n = 12$)

LONG RANGE ATTRACTIONS

- DISPERSION (NEUTRAL PARTICLES) 10^{-2} eV

$$V_D(r_{ij}) = -C_{ij}\, r_{ij}^{-6} = -4\varepsilon_{ij}\left(\frac{\sigma_{ij}}{r_{ij}}\right)^6$$

σ, ε LENNARD-JONES PARAMETERS $V_{LJ} = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{R}\right)\right.$

- IONIC (CHARGED PARTICLES) 1 eV

$$V_I(r_{ij}) = q_i\, q_j\, r_{ij}^{-1}$$

- POLARIZATION (CHARGED PARTICLE - NEUTRAL PARTICLE) 10^{-1} eV

$$V_P(r_{ij}) = f(r_{ij})\, \frac{\alpha_i}{2} q_j^2\, r_{ij}^{-4} \quad \text{(charge-dipole)}$$

SWITCHING FUNCTION $f(r) = 1 - \exp\left[-\left(\frac{r}{r_c}\right)^6\right]$

correct for short range INACCURACY OF POINT CHARGE - POINT DIPOLE APPROXIMATION

USUALLY WITH COMBINATION RULES

$$A_{\alpha\beta} = \sqrt{A_{\alpha\alpha} A_{\beta\beta}} \qquad \sigma_{\alpha\beta} = \left(\frac{\sigma_\alpha + \sigma_\beta}{2}\right)$$

$$C_{\alpha\beta} = \sqrt{C_{\alpha\alpha}\, C_{\alpha\beta}}$$

CHARACTERISTICS

- BONDED
  - FIXED BOND TOPOLOGY
  - SHORT RANGE - MANY BODY $O(N)$
  - FAST DYNAMICS (require timestep $0.5 \div 1$ fs)

- NON BONDED
  - LONG RANGE, MANY BODY $O(N^2)$ *
  - VARIABLE BOND TOPOLOGY
  - SLOW DYNAMICS (require timestep $5 \div 10$ fs)

OPTIMAL TREATMENT OF FORCES IN MD REQUIRE DIFFERENT APPROACHES FOR BONDED AND NON BONDED INTERACTIONS

BONDED INTERACTIONS ⟷ TIME SCALE PROBLEM

○ MULTIPLE TIME STEPS ○ CONSTRAINTS

NON BONDED INTERACTIONS ⟷ SPACE SCALE PROBLEM

- $O(N)$ methods for search of pairs
  - VERLET LIST
  - LINKED CELL

- CORRECT TREATMENT OF COULOMBIC INTERACTIONS IN PERIODIC SYSTEMS
  - EWALD SUM
  - FAST MULTIPOLE METHOD

- SELF CONSISTENCY FOR POLARIZATION SCHEMES

MOLECULAR DYNAMICS OF CONSTRAINED SYSTEMS

CHARACTERISTIC FREQUENCY OF C-H STRETCHING IN AN ALKANE CHAIN 2900 cm^{-1}

REASONABLE INTEGRATION WITH VERLET SCHEME REQUIRES δt AS SMALL AS .5 fs OR LESS

DYNAMICS OF TORSION - THE INTERESTING CONFORMATIONAL DYNAMICS - CAN BE FOLLOWED WITH $\delta t \sim 10$ fs WITHOUT LOSS OF PRECISION.

SOLUTION: TREAT BONDS AS RIGID

INSTEAD OF A STRETCHING HARMONIC POTENTIAL

$$V_{bond}(r_{ij}) = \frac{k_b}{2}(r_{ij} - b_o)^2$$

APPLY A HOLONOMIC CONSTRAINTS TO THE SYSTEM

$$\sigma(r_{ij}) = r_{ij}^2 - b_o^2 = 0$$

CLASSICAL MECHANICS OF LAGRANGIAN SYSTEM IN THE PRESENCE OF HOLONOMIC CONSTRAINTS

- Lagrangian equations of motion for uncostrained system

$$\frac{d}{dt}\frac{\partial \mathcal{L}}{\partial \dot{\mathbf{r}}} = \frac{\partial \mathcal{L}}{\partial \mathbf{r}} \quad ; \quad \mathcal{L} = K - V$$

- CONSTRAINTS relations

$$\sigma_k(\{\mathbf{r}\}) = 0$$

INTRODUCE A NEW LAGRANGIAN

$$\mathcal{L}' = \mathcal{L} - \sum_k \lambda_k \sigma_k$$

$\{\lambda_k\}$ set of undetermined LAGRANGE MULTIPLIERS

CORRESPONDING CONSTRAINED EQ.S OF MOTION

$$\frac{d}{dt}\frac{\partial \mathcal{L}'}{\partial \dot{r}_i} = \frac{\partial \mathcal{L}'}{\partial r_i} = \frac{\partial \mathcal{L}}{\partial r_i} - \sum_k \lambda_k \frac{\partial \sigma_k}{\partial r_i}$$

or

$$m_i \ddot{r}_i = -\frac{\partial V}{\partial r_i} - \sum_k \lambda_k \frac{\partial \sigma_k}{\partial r_i}$$

$$= F_i + \sum_k G_i^{(k)}$$

CONSTRAINT FORCES $G_i^{(k)}$ UNKNOWN : SOLVE FOR λ_k

$$\frac{d^2}{dt^2}\sigma_k = \frac{d}{dt}\dot{\sigma}_k = \frac{d}{dt}\left(\frac{\partial \sigma_k}{\partial r}\cdot\frac{dr}{dt}\right) = 0$$

$$0 = \frac{\partial}{\partial r}\left(\frac{\partial \sigma_k}{\partial r}\right) : \frac{dr}{dt}\,\frac{dr}{dt} + \frac{d^2 r}{dt^2}\cdot\frac{\partial \sigma_k}{\partial r}$$

SUBSTITUTING FOR $\ddot{r}$ ONE GETS A LINEAR SYSTEMS IN THE UNKNOWN λ_k

$$\sum_{i=1}^{N} \frac{1}{m_i} F_i \cdot \frac{\partial \sigma_k}{\partial r_i} - \sum_{i=1}^{N} \frac{1}{m_i} \sum_{\ell} \lambda_\ell \frac{\partial \sigma_\ell}{\partial r_i}\cdot\frac{\partial \sigma_k}{\partial r_i}$$

$$+ \sum_{i,j} \left(\dot{r}_i \cdot \frac{\partial}{\partial r_i}\right)\left(\dot{r}_j \cdot \frac{\partial}{\partial r_j}\right)\sigma_k = 0$$

THAT IS IN MATRIX NOTATION

$$\mathcal{F}_k - \Lambda_\ell M_{k\ell} + \mathcal{T}_k = 0$$

whose FORMAL SOLUTIONS is

$$\Lambda = M^{-1}\left(\mathcal{F} + \mathcal{T}\right)$$

SOLUTION FOR UNKNOWN MULTIPLIER

$$\lambda_k = \lambda_k\left(r_i\, , \dot{r}_i\, , F_i\right)$$

NUMERICAL INSTABILITY :

- CONSTRAINTS ARE SATISFIED WITHIN THE TYPICAL ERROR OF THE NUMERICAL INTEGRATION SCHEME
- ERRORS PROPAGATE AND DUE TO EXPONENTIAL DIVERGENCE OF TRAJECTORY CONSTRAINTS QUICKLY BECOME NO LONGER SATISFIED

A SIMPLE EXAMPLE

PARTICLE CONSTRAINED TO MOVE ON A SPHERE of RADIUS d

$$\sigma = \frac{1}{2}\left(r^2 - d^2\right)$$

$$G = -\lambda \frac{\partial \sigma}{\partial r} = -\lambda r$$

$$\ddot{\sigma} = 0 \quad \Rightarrow \quad \ddot{r} \cdot r + \dot{r}^2 = 0$$

$$\ddot{r} = \frac{1}{m}(F + G) = \frac{1}{m}(F - \lambda r)$$

In the absence of external forces $(F = 0)$

$$-\frac{\lambda}{m} r^2 + \dot{r}^2 = 0 \quad \Rightarrow \quad \lambda = \frac{m\dot{r}^2}{r^2}$$

The CONSTRAINT FORCE $G = -\lambda \vec{r} = -m\dot{r}^2 \dfrac{\vec{r}}{r^2}$

in terms of angular velocity $\dot{r} = \omega r$

$G = -m\omega^2 \vec{r}$ (well Know centripetal force)

using the Verlet scheme

$$\vec{r}(t + \delta t) = 2\vec{r}(t) - \vec{r}(t - \delta t) - \omega^2 \delta t^2 \vec{r}(t)$$

WHAT IS THE ERROR ON THE CONSTRAINT ?

$$\begin{aligned}
r^2(t + \delta t) &= 4\, r(t)^2 + r(t - \delta t)^2 + \omega^4 \delta t^4\, r(t)^2 \\
&\quad - 4\, \vec{r}(t) \cdot \vec{r}(t - \delta t) - 4\omega^2 \delta t^2\, r(t)^2 \\
&\quad + 2\omega^2 \delta t^2\, r(t) \cdot r(t - \delta t) \\
&= d^2\left(5 + \omega^4 \delta t^4 - 4\omega^2 \delta t^2\right) + r(t) \cdot r(t - \delta t)\left(2\omega^2 \delta t^2 - 4\right. \\
&= d^2 \left(5 + \omega^4 \delta t^4 - 4\omega^2 \delta t^2 + \cos(\omega \delta t)(2\omega^2 \delta t^2 - 4)\right. \\
&\simeq d^2 \left(1 - \frac{(\omega \delta t)^4}{6} + O(\Delta t^6)\right)
\end{aligned}$$

THE CONSTRAINTS IS SATISFIED WITHIN THE ERROR $O(\delta t^4)$ OF THE ALGHORITHM

SOLUTION TO THE NUMERICAL PROBLEM

COMPUTE THE UNKNOWN LAGRANGE MULTIPLIER IN SUCH AWAY AS THE CONSTRAINT BE SATISFIED <u>AT ALL TIMES</u>

THE EXACT LAGRANGE MULTIPLIER λ_K ARE REPLACED BY ASET OF VALUES γ_K such THAT

$$\sigma_K(\{r(t+\delta t)\}) = 0$$

$\{\gamma_K\}$ DIFFER FROM $\{\lambda_K\}$ BY QUANTITIES OF THE ORDER OF THE ERROR IN THE ALGORITHM.

IMPLEMENTATION IN THE VELOCITY VERLET SCHEME

FIRST STEP:

$$\vec{r}_i(t+\delta t) = \vec{r}_i(t) + \vec{v}_i(t)\,\delta t + \frac{\delta t^2}{2m_i}\vec{f}_i + \frac{\delta t^2}{2m_i}\vec{g}_i(\gamma_K)$$

$$\vec{r}_i(t+\delta t) = \vec{r}_i{}'(t+\delta t) + \frac{\delta t^2}{2m_i}\vec{g}_i(\gamma_K)$$

CONSTRAINT RELATIONS AT TIME $t+\delta t$

$$\sigma_K\left(\left\{r_i'(t+\delta t) + \frac{\delta t^2}{2m_i}\vec{g}_i(\gamma_K)\right\}\right) = 0$$

THIS IS A SYSTEM OF (NON LINEAR) EQUATIONS IN THE UNKNOW $\{\gamma_K\}$. SOLUTION CAN BE ACHIEVED WITH AN ITERATIVE PROCEDURE KNOWN AS "SHAKE".

SECOND STEP:

$$\vec{v}_i(t+\delta t) = \vec{v}_i(t) + \frac{\delta t}{2m_i}\left[\left(\vec{f}_i(t) + \vec{g}_i(t)\right) + \left(\vec{f}_i(t+\delta t) + \vec{g}_i(t+\delta t)\right)\right]$$

$$\vec{v}_i(t+\delta t) = \vec{v}_i{}'(t+\delta t) + \frac{\delta t}{2m_i}\vec{g}_i(t+\delta t)$$

TO COMPLETE THE SOLUTION ONE NEEDS TO FIND THE CONSTRAINT FORCES AT TIME $t+\delta t$ $\vec{g}_i(t+\delta t)$, i.e. a new set of MULTIPLIER $\{\mu_K\}$ FROM THE RELATIONS

$$\dot{\sigma}_K(t+\delta t) = \sum_{i=1}^{N}\left(\vec{v}_i{}'(t+\delta t) + \frac{\delta t}{2m_i}\vec{g}_i(\mu_K)\right) \cdot \frac{\partial \sigma_K}{\partial \vec{r}_i}\left(\vec{r}_i(t+\delta t)\right)$$

THIS IS AGAIN A SYSTEM OF EQUATIONS IN THE UNKNOWN μ_k. SOLUTION CAN BE ACHIEVED WITH THE SAME ITERATIVE PROCEDURE. THE ADAPTATION TO $\dot{\sigma}_k$ IS OFTEN REFERRED TO AS "RATTLE"

ITERATIVE SOLUTION FOR THE UNKNOWN γ_k

$$r_i^{(c)}(t+\delta t) = r_i^{(u)}(t+\delta t) + \frac{\delta t^2}{2m_i}\sum_k \gamma_k \frac{\partial \sigma_k(t)}{\partial \vec{r}_i}$$

FIRST ORDER ESPANSION OF $\sigma_k(t+\delta t)$

$$\sigma_k(t+\delta t) = \sigma_k\left(r^{(u)}(t+\delta t)\right) + \sum_{i=1}^{N}\left(\frac{\partial \sigma_k}{\partial \vec{r}_i}\right)_{r_i^{(u)}} \cdot \left(\vec{r}_i^{\,(c)} - \vec{r}_i^{\,(u)}\right) + O(\delta t^4) = 0$$

AN ITERATIVE SOLUTION CAN BE FOUND SOLVING THIS SYSTEM OF LINEAR EQUATIONS IN $\{\gamma_k\}$ [MATRIX METHOD] IT REQUIRES A MATRIX INVERSION THAT CAN BE EXPENSIVE

ALTERNATIVE : "SHAKE"

$$r_i^{(c)}(t+\delta t) - r_i^{(u)}(t+\delta t) \simeq \frac{\delta t^2}{2m_i}\gamma_k \frac{\partial \sigma_k(t)}{\partial \vec{r}_i}$$

ONE CONSIDER THE EFFECT OF A SINGLE CONSTRAINT AT A TIME

$$\sigma_k\left(r^{(u)}(t+\delta t)\right) = \frac{\delta t^2}{2}\gamma_k \sum_{i=1}^{N} \frac{1}{m_i} \frac{\partial \sigma_k(t+\delta t)}{\partial \vec{r}_i} \cdot \frac{\partial \sigma_k(t)}{\partial \vec{r}_i}$$

AND OBTAINS FOR γ_k AN ESTIMATE

$$\overline{\gamma}_k \frac{\delta t^2}{2} = \sigma\left(r^{(u)}(t+\delta t)\right) \Big/ \Big[\sum_{i=1}^{N} \frac{1}{m_i} \frac{\partial \sigma_k(t+\delta t)}{\partial \vec{r}_i} \cdot \frac{\partial \sigma_k(t)}{\partial \vec{r}_i}$$

CONSTRAINTS ARE CONSIDERED IN SUCCESSION SOLVING ONE AT A TIME. THE PROCEDURE IS ITERATED CORRECTING $r_i(t+\delta t)$ WITH THE OBTAINED $\overline{\gamma}_k$ ESTIMATES UNTIL THE REQUIRED PRECISION IS REACHED IN THE CONSTRAINT RELATIONS AT TIME $t+\delta t$

AVERAGES IN CONSTRAINED ENSEMBLE

SINCE $\sigma_k(r(t)) = 0$ ALSO $\dot{\sigma}_k(r(t), \dot{r}(t)) = 0$

RELATION INVOLVING COORDINATES REL. INVOLVING COORDINATES & MOMENTA

IN THE ENSEMBLE AVERAGES APPEAR A CORRECTING TERM ALSO FOR MOMENTUM DISTRIBUTION.

THIS RESULT IN A DIFFERENCE BETWEEN AVERAGES IN A CONSTRAINED ENSEMBLE WITH RESPECT TO THE ENSEMBLE CORRESPONDING TO A SYSTEM WITH HARMONIC SPRING POTENTIAL EVEN IN THE LIMIT $K \to \infty$ OF INFINITELY STIFF SPRINGS.

USING GENERALISED COORDINATES THE SYSTEM CAN BE DIVIDED IN TWO PARTS:

$\{q_s\}$ SET OF "SOFT" COORDINATES

$\{q_H\}$ SET OF "HARD" COORDINATES

"HARD" COORDINATES ARE EVENTUALLY REPLACED BY CONSTRAINTS $\{q_H\} = \{\sigma_k\}$

SYSTEM WITH STIFF SPRINGS

$$u(q) = u(q_s, q_H) \qquad U = U_H(q_s) = U(q_s; \sigma_k)$$

$$\mathcal{L} = \frac{1}{2}\sum m_i \dot{q}_\alpha \frac{\partial \vec{r}_i}{\partial q_\alpha} \cdot \frac{\partial \vec{r}_i}{\partial q_\beta} \dot{q}_\beta - U \qquad \mathcal{L}^{(H)} = \frac{1}{2}\sum m_i \dot{q}^{(s)}_\alpha \frac{\partial \vec{r}_i}{\partial q^{(s)}_\alpha} \frac{\partial \vec{r}_i}{\partial q^{(s)}_\beta} \dot{q}^{(s)}_\beta - U$$

$$= \frac{1}{2}\dot{q}\,\underline{\underline{G}}\,\dot{q} - U \qquad = \frac{1}{2}\dot{q}_s \cdot \underline{\underline{G_s}} \cdot \dot{q}_s - U(q_s;\sigma)$$

$$p_\alpha = \frac{\partial \mathcal{L}}{\partial \dot{q}_\alpha} = G_{\alpha\beta}\dot{q}_\beta \qquad p^{(s)}_\alpha = \frac{\partial \mathcal{L}^{(H)}}{\partial \dot{q}^{(s)}_\alpha} = (G_s)_{\alpha\beta}\dot{q}^{(s)}_\beta$$

$$\mathcal{H} = \frac{1}{2}p \cdot \underline{\underline{G}}^{-1} \cdot p + U(q) \qquad \mathcal{H}^{(H)} = \frac{1}{2}p_s \cdot \underline{\underline{G_s}}^{-1} \cdot p_s + U(q_s;\sigma_k)$$

CANONICAL DISTRIBUTION FOR COORDINATE {q}

STIFF SPRING

$$\rho(q) = \frac{1}{Q_{NVT}} \int dp \exp\left\{-\beta \left[\frac{1}{2}\, p \cdot \underline{\underline{G}}^{-1} \cdot p + U(q)\right]\right\}$$

$$\propto \quad \exp\{-\beta U(q)\} \sqrt{|\underline{\underline{G}}|}$$

$|\underline{\underline{G}}|$ ABSOLUTE VALUE OF THE DETERMINANT OF MATRIX

SYSTEM WITH CONSTRAINTS

$$\rho_H(q_s) = \frac{1}{Q^{(s)}_{NVT}} \int dp_s \exp\left\{-\beta \left[\frac{1}{2}\, p_s \cdot \underline{\underline{G}}_s^{-1} \cdot p_s + U(q_s;\sigma_k)\right]\right\}$$

$$\propto \quad \exp\{-\beta U(q_s;\sigma_k)\} \sqrt{|\underline{\underline{G}}_s|}$$

IN THE INFINITELY STIFF SPRINGS LIMIT $K \to \infty$

$$\rho_H(q_s)/\rho(q_s, q_H = \sigma) = \sqrt{|\underline{\underline{G}}_s| / |\underline{\underline{G}}|}$$

$$\left(G^{-1}\right)_{\alpha\beta} = \sum_{i=1}^{N} \frac{1}{m_i} \frac{\partial q_\alpha}{\partial \vec{r}_i} \cdot \frac{\partial q_\beta}{\partial \vec{r}_i}$$

IN BLOCK FORM

$$\underline{\underline{G}} = \left(\begin{array}{c:c} \underline{\underline{G}}_S & \underline{\underline{A}}_{SH} \\ \hdashline \underline{\underline{A}}_{HS} & \underline{\underline{A}}_{HH} \end{array}\right) \qquad \underline{\underline{G}}^{-1} = \left(\begin{array}{c:c} \underline{\underline{B}}_{SS} & \underline{\underline{B}}_{SH} \\ \hdashline \underline{\underline{B}}_{HS} & \underline{\underline{Z}} \end{array}\right)$$

WHERE $\underline{\underline{Z}}$ IS RELATIVE TO THE CONSTRAINED COORDINATES

$$(Z)_{\alpha\beta} = \sum_{i=1}^{N} \frac{1}{m_i} \frac{\partial \sigma_\alpha}{\partial \vec{r}_i} \cdot \frac{\partial \sigma_\beta}{\partial \vec{r}_i}$$

DEFINING A MATRIX $\underline{\underline{X}}$ AS $\underline{\underline{X}} = \left(\begin{array}{c:c} \underline{\underline{G}}_S & \underline{\underline{0}} \\ \hdashline \underline{\underline{A}}_{HS} & \underline{\underline{I}} \end{array}\right)$

$(\det(\underline{\underline{X}}) = \det(\underline{\underline{G}}_s))$

ONE OBTAINS $\underline{\underline{G}}\,\underline{\underline{G}}^{-1}\underline{\underline{X}} = \underline{\underline{G}} \left(\begin{array}{c:c} \underline{\underline{I}} & \underline{\underline{B}}_{SH} \\ \hdashline \underline{\underline{0}} & \underline{\underline{Z}} \end{array}\right)$

AND FOR DETERMINANTS

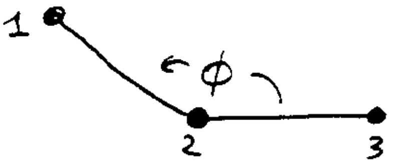
$$|\underline{\underline{X}}| = |\underline{\underline{G}}_s| = |\underline{\underline{G}}\,\underline{\underline{G}}^{-1}\underline{\underline{X}}| = |\underline{\underline{G}}|\,|\underline{\underline{Z}}|$$

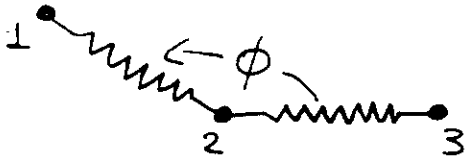
OR $\boxed{|\underline{\underline{Z}}| = |\underline{\underline{G}}| / |\underline{\underline{G}}_s|}$

RELATIONSHIP BETWEEN COORDINATE ENSEMBLE DISTRIBUTIONS

$$\rho(q) = \sqrt{|Z|}\;\rho_H(q_s;\sigma)$$

EXAMPLE : TRIATOMIC MOLECULE WITH EQUAL MASSES m





CONSTRAINED SYSTEM

STIFF SPRINGS

$$\sigma_1 = |\vec{r}_1 - \vec{r}_2|^2 - d^2$$

$$\sigma_2 = |\vec{r}_2 - \vec{r}_3|^2 - d^2$$

$$U = \frac{k}{2}\left[\left(|\vec{r}_1 - \vec{r}_2| - d\right)^2 + \left(|\vec{r}_2 - \vec{r}_3| - d\right)^2\right.$$

$$|\underline{\underline{Z}}| = \frac{4}{m}\begin{vmatrix} 2\,r_{12}^2 & -\vec{r}_{12}\cdot\vec{r}_{13} \\ -\vec{r}_{12}\cdot\vec{r}_{23} & 2\,r_{23}^2 \end{vmatrix}$$

$$= \frac{4}{m}\left(4\,r_{12}^2 r_{23}^2 - (\vec{r}_{12}\cdot\vec{r}_{23})^2\right)$$

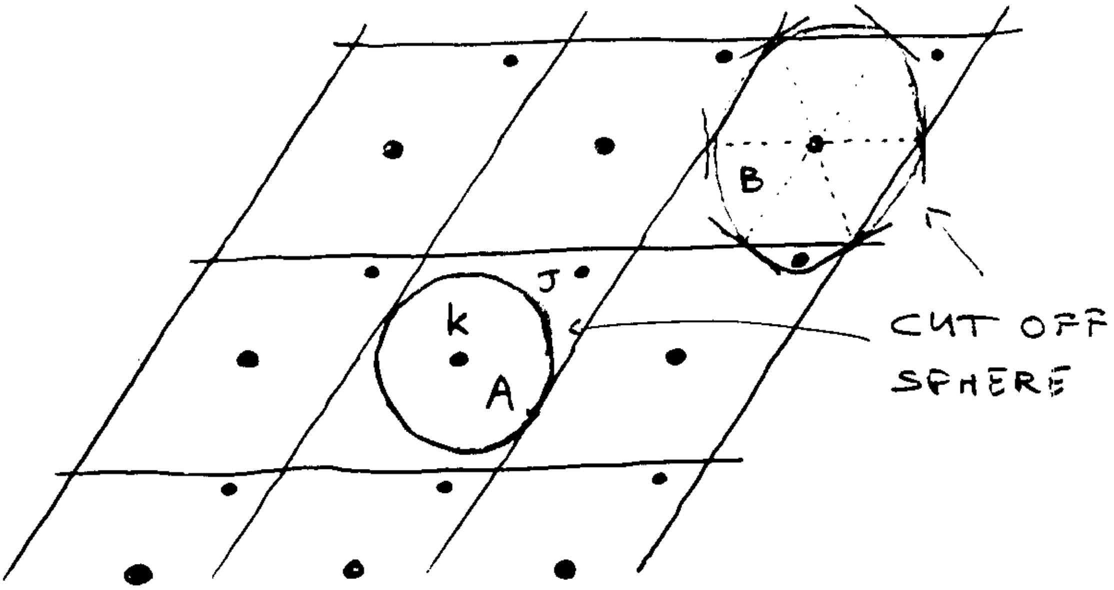
$$= \frac{(2d)^4}{m}\left(1 - \frac{\cos^2\phi}{4}\right)$$

ONE OBTAIN FOR THE EQUILIBRIUM DISTRIBUTION OF THE ANGLE ϕ IN THE ABSENCE OF EXTERNAL FORCES A DIFFERENT RESULT

$$\frac{\rho_{\mathrm{SPRING}}}{\rho_{\mathrm{HARD}}} = c\sqrt{1 - \frac{\cos^2\phi}{4}}$$

PERIODIC BOUNDARY CONDITIONS

MINIMUM IMAGE CONVENTION



k - J pair

MINIMUM DISTANCE r_{kJ} between any two IMAGE

$\vec{r}_i \rightarrow \vec{\rho}_i$ TRASFORMATION OF THE TRICLINIC CELL TO THE UNIT CUBE

MINIMUM ρ_{kj}

for each COMPONENT $(\vec{\rho}_k - \vec{\rho}_J) - \mathrm{NINT}(\vec{\rho}_k - \vec{\rho}_J) = \vec{d}_{kJ}$

with this choice each component $\left|(\vec{d}_{kJ})_\alpha\right| \leq 0.5$

THIS is THE MINIMUM IMAGE ONLY FOR

CASE A - LARGEST SPHERE INSCRIBED IN MD CELL

WRONG ANSWER (FOR SOME PAIRS) FOR CASE B

- LARGEST SPHERE INSCRIBED IN WIGNER-SEITZ CELL

PRESSURE IN MOLECULAR SYSTEMS
(WITH CONSTRAINTS)

THE DEFINITION OF THE "INTERNAL PRESSURE" AS AVERAGE OF THE RELEVANT MICROSCOPIC OBSERVABLE CAN BE DONE IN TWO EQUIVALENT MODES

"Atomic" DEFINITION

$$P = \left\langle \frac{1}{3V} \sum_{i=1}^{N} \left(\frac{p_i^2}{2m_i} + \vec{r}_i \cdot \vec{f}_i \right) \right\rangle$$

WHERE $\vec{f}_i$ <u>MUST</u> CONTAIN ALSO THE CONSTRAINT FORCE.

"MOLECULAR DEFINITION"

$$P = \left\langle \frac{1}{3V} \sum_{\alpha=1}^{M} \frac{P_\alpha^2}{2M_\alpha} + \vec{R}_\alpha \cdot \vec{F}_\alpha \right\rangle$$

FOR M molecules with CENTER OF MASS $\vec{R}_\alpha, \vec{P}_\alpha, \vec{F}_\alpha$
(CONSTRAINT FORCES CANCEL OUT)

PROBLEMS IN A PERIODIC SYSTEM

THE POTENTIAL CONTRIBUTION IN THE PRESENCE OF PERIODIC BOUNDARY AND USING MINIMUM IMAGE CONVENTION REQUIRES SPECIAL CARE...

$$\sum_i \vec{r}_i \cdot \vec{F}_i = \sum_{i>j} \vec{r}_{ij} \cdot \vec{f}_{ij}$$

$\vec{f}_{ij}$ force ON ATOM i DUE TO ATOM J $\left(= - \vec{f}_{ji} \right)$

$\vec{r}_{ij}$ and $\vec{f}_{ij}$ MUST BE <u>COHERENT</u>

THAT IS COMPUTED ON THE SAME PAIR OF IMAGES.

A SIMILAR FORMULATION CAN BE DONE IN THE "MOLECULAR" CASE.

Stress Tensor: molecular vs atomic formulation

$$T^{xz} = \sum_{\alpha=1}^{N} x_\alpha F^z_\alpha$$

$$T^{xz} = \sum_{\alpha=1}^{N} \sum_{i=1}^{n} x_\alpha F^z_{i\alpha} = \sum_{\alpha=1}^{N} \sum_{i=1}^{n} x_\alpha \sum_{\alpha\neq\beta=1}^{N} \sum_{j=1}^{n} F^z_{i\alpha j\beta}$$

$$= \sum_{\alpha\neq\beta=1}^{N} \sum_{i,j=1}^{n} x_\alpha F^z_{i\alpha j\beta} = \sum_{\alpha,\beta>\alpha=1}^{N} \sum_{i,j=1}^{n} (x_\alpha - x_\beta) F^z_{i\alpha j\beta}$$

$$F^z_{i\alpha j\beta} = -F^z_{j\beta i\alpha}$$

$$T^{xz} = \sum_{\alpha,\beta>\alpha=1}^{N} \sum_{i,j=1}^{n} (x_{i\alpha} - x_{j\beta}) F^z_{i\alpha j\beta}$$

$$+ \sum_{\alpha,\beta>\alpha=1}^{N} \sum_{i,j=1}^{n} [(x_\alpha - x_{i\alpha}) - (x_\beta - x_{j\beta})] F^z_{i\alpha j\beta}$$

$$T^{xz} = \sum_{\alpha,\beta>\alpha=1}^{N} \sum_{i,j=1}^{n} (x_{i\alpha} - x_{j\beta}) F^z_{i\alpha j\beta}$$

$$- \sum_{\alpha=1}^{N} \sum_{i=1}^{n} (x_{i\alpha} - x_\alpha) \sum_{\beta\neq\alpha=1}^{N} \sum_{j=1}^{n} F^z_{i\alpha j\beta}$$

Ensemble method: NPT Equations of motion

In standard molecular dynamics simulation, we usually consider the time evolution of a classical system composed of a fixed number N of particles in a periodically repeated volume V, whose shape and size is fixed. The state of the system is completely determined by the $3N$ coordinates $\{\vec{r}^N\} = \{\vec{r}_i, i = 1, \ldots, N\}$ and $3N$ momenta $\{\vec{p}^N\} = \{\vec{p}_i, i = 1, \ldots, N\}$, and its dynamics by the hamiltonian $\mathcal{H}$

$$\mathcal{H}(\vec{r}^N, \vec{p}^N) = \sum_{i=1}^{N} \frac{\vec{p}_i^2}{2m_i} + \mathcal{V}(\vec{r}^N) = \mathcal{K}(\vec{p}^N) + \mathcal{V}(\vec{r}^N) \tag{1}$$

where m_i is the mass of the i^{th} particle and $\mathcal{V}(\vec{r}^N)$ is the potential energy. In the absence of external perturbations, the total energy $E = \mathcal{H}(\vec{r}^N, \vec{p}^N)$ of the system is conserved. Therefore, averaging over the time and making use of the ergodic hypothesis, one can obtain macroscopic properties relative to constant N, V, E conditions, i.e. corresponding to the microcanonical ensemble of statistical mechanics. In particular, the temperature and pressure of the simulation cannot be fixed but can only be estimated by making use of the equipartition theorem

$$T = \frac{2}{3Nk_{\mathrm{B}}} \left\langle \sum_{i=1}^{N} \frac{\vec{p}_i^2}{2m_i} \right\rangle_t \tag{2}$$

and the virial theorem

$$P = \frac{1}{3V} \left\langle \sum_{i=1}^{N} \frac{\vec{p}_i^2}{m_i} + \vec{r}_i \cdot \vec{F}_i \right\rangle_t, \quad \vec{F}_i = -\frac{\partial \mathcal{V}(\vec{r}^N)}{\partial \vec{r}_i} \tag{3}$$

where $\langle \ldots \rangle_t$ stands for the average over the finite time trajectory generated by numerical integration of the equations of motion. Therefore only after the simulation is done can one know at what temperature and pressure it has been carried out. When studying the phase behaviour of a system this can be a major drawback of molecular dynamics with respect to the Monte Carlo method, which, however, does not yield any dynamical information.

From statistical mechanics we know that to produce a new ensemble one has simply to couple weakly the system of interest with a suitable reservoir. The way this is achieved theoretically, however, is not applicable to molecular dynamics simulation. The reservoir is usually a virtually infinite system with many more degrees of freedom than the system of interest, and the coupling is done through surfaces, becoming infinitely small in the thermodynamic limit. In simulation we really do not want to spend time integrating non-interesting degrees of freedom, and periodic boundary conditions are usually employed just to get rid of unwanted surfaces when studying bulk samples.

The key idea of Andersen's 1980 paper [1] is that MD reservoirs can be represented by only one or a few degrees of freedom, and the coupling can be applied uniformly to all particles. This is done by inventing new equations of motion for the extended system, composed of the system of interest plus the required reservoirs. These equations are derived by a Lagrangian, or in Hamilton's canonical form, only in a *virtual* system of coordinates and become non-canonical when expressed in term of the *real* variables of the system of interest. The particular form of these equations is chosen in such a way that the microcanonical equilibrium distribution produced by a constant-energy trajectory of the extended system reduces to the desired distribution when the coordinates and momenta of the system of interest are considered, that is after integration over the extra reservoir variables.

The extended system lagrangian, introduced by Andersen, was designed to produce a constant pressure, constant enthalpy simulation by adding one extra variable, representing the MD cell volume, which is therefore free to fluctuate, and the coupling is made through a dynamical equation of motion for the cell volume variable. When the cell volume changes there is a uniform spatial scaling of the particle positions.

In the same paper a constant-temperature method was also introduced. This, however, was based on a different mechanism in which the coupling between the heat reservoir and the system of interest is stochastic and is implemented by randomly sampling particle velocities from a maxwellian distribution. This method is of relevance when dealing with complex systems where there is a poor coupling between various degrees of freedom, for example molecular internal vibrational and translational or rotational degrees of freedom, and it is probably the best method of achieving adequate equilibrium sampling in these systems.

For constant temperature we shall focus our attention on the method first proposed by Nosé [2], and later clarified by Hoover [3] and Nosé himself [4], referring the interested reader to his latest review article for a more detailed and fully comprehensive treatment of constant-temperature molecular dynamics methods [5]. Once again the reservoir is described by a single degree of freedom, which however does not have a simple physical meaning [6], and the coupling contains a scaling term which applies uniformly to all particle velocities and is in fact a scaling on simulation time. Hoover's approach simplifies matters as it does not require the use of *virtual* variables and scaling concepts and also makes a direct link to constraint methods.

Finally the so-called Parrinello-Rahman method [7] deserve to be mentioned on its own. In this method the pressure reservoir is represented by a set of nine variables which describe the complete geometry of the MD cell, thus allowing fluctuations of both its volume and shape. This is essential in the study of phase stability and phase transformations in solid systems.

Andersen's demon

Rather than follow the original demonstration by Andersen for the NPH ensemble we shall combine it with the Nosé derivation and consider directly the case of the NPT ensemble. As a word of caution, it must be mentioned that different lagrangians can be set up, all leading to the same equilibrium distribution but with different definitions and dynamics for the reservoir variables.

Virtual-variable representation

In the constant-pressure molecular dynamics method the volume V of the MD box is allowed to fluctuate in time. Andersen replaces the atomic coordinates $\{\vec{r}_i, i = 1, \ldots, N\}$ with *virtual* scaled coordinates $\{\vec{\rho}_i, i = 1, \ldots, N\}$ defined in the following way.

$$\vec{\rho}_i = V^{-1/3}\vec{r}_i. \tag{4}$$

Each component of $\{\vec{\rho}_i, i = 1, ..., 3N\}$ is therefore a dimensionless number between zero and one (taking care to consider always the image inside the MD box).

Similarly Nosé introduces a scaled time τ which is related to the *real* one through the reservoir coordinate s in the following way

$$\mathrm{d}\tau = s\mathrm{d}t. \tag{5}$$

This implies some caution is needed when considering relations between time derivatives. In fact

$$\frac{\mathrm{d}\vec{\rho}_i}{\mathrm{d}\tau} = \frac{\mathrm{d}\left(\vec{r}_i V^{-1/3}\right)}{s\mathrm{d}t} \Rightarrow \frac{\mathrm{d}\vec{r}_i}{\mathrm{d}t} = V^{1/3}s\frac{\mathrm{d}\vec{\rho}_i}{\mathrm{d}\tau} + \frac{\vec{r}_i}{3V}\frac{\mathrm{d}V}{\mathrm{d}t}. \tag{6}$$

We can now introduce the following Lagrangian for the extended system [8]

$$\begin{aligned}\mathcal{L} &= \sum_{i=1}^{N} \frac{1}{2} m_i Q^{2/3} S^2 \dot{\vec{\rho}}_i \cdot \dot{\vec{\rho}}_i - \mathcal{V}(\{\vec{\rho}_i Q^{1/3}, i = 1, \ldots, N\}) \\ &+ \frac{1}{2} S^2 M_Q \dot{Q}^2 - P_{\text{ext}} Q + \frac{1}{2} M_S \dot{S}^2 - g k_{\text{B}} T \ln S \end{aligned} \tag{7}$$

in which the two new variables Q and S appear. If we interpret Q as the volume V then the two terms on the first line are just the lagrangian of the system of interest. The second line contains the new terms. First a kinetic energy term, followed by a potential energy term for the motion of Q in which two constants appear, the inertia factor M_Q and the external pressure P_{ext}. The third term is the kinetic term for the Nosé variable S, and the fourth the corresponding potential energy term. The constants appearing there are another inertia factor M_S and the temperature of the reservoir with Boltzmann constant $k_{\text{B}}T$, while g is the number of degrees of freedom which are in contact with the heat reservoir and, as shown later, it depends on the system studied.

Let us recall Andersen's physical interpretation of the Q terms. Imagine that the fluid to be simulated can be compressed in a container whose volume is changed by a piston. Thus M_Q represents the mass of the piston whose motion is described by the coordinate Q, and $P_{\text{ext}}Q$ is the potential derived from an external pressure P_{ext} acting on the piston. The piston is a *virtual* one and produces an isotropic expansion or contraction of the fluid. This interpretation is not completely consistent as, writing down the expected particle velocities

$$\dot{\vec{r}}_i = \dot{\vec{\rho}}_i Q^{-1/3} + \frac{1}{3} \vec{\rho}_i \dot{Q} Q^{-2/3} \tag{8}$$

one finds that the second term of this derivative does not appear in the kinetic terms of the lagrangian.

Hamiltonian equations of motion

However eqn (7) gives a well-defined Lagrangian for the extended system in terms of *virtual* coordinates. The next step is therefore to derive from it the conjugate momenta. First the momenta conjugate to the particle coordinates $\vec{\rho}_i$ will be denoted $\vec{\pi}_i$

$$\vec{\pi}_i = \frac{\partial \mathcal{L}}{\partial \dot{\vec{\rho}}_i} = m_i S^2 Q^{2/3} \dot{\vec{\rho}}_i . \tag{9}$$

The momentum conjugate to Q will be denoted Π_Q

$$\Pi_Q = \frac{\partial \mathcal{L}}{\partial \dot{Q}} = M_Q S^2 \dot{Q} \tag{10}$$

and the momentum conjugate to S will be denoted Π_S

$$\Pi_S = \frac{\partial \mathcal{L}}{\partial \dot{S}} = M_S \dot{S}. \tag{11}$$

The hamiltonian of the extended system can now be written down

$$\begin{aligned} \mathcal{H} &= \sum_{i=1}^{N} \dot{\vec{\rho}}_i \cdot \vec{\pi}_i + \dot{Q}\Pi_Q + \dot{S}\Pi_S - \mathcal{L} \\ &= \sum_{i=1}^{N} \frac{\vec{\pi}_i \cdot \vec{\pi}_i}{2m_i S^2 Q^{2/3}} + \mathcal{V}(\{\vec{\rho}_i Q^{1/3}, i = 1, \ldots, N\}) \\ &\quad + \frac{\Pi_Q^2}{2M_Q S^2} + P_{\text{ext}} Q + \frac{\Pi_S^2}{2M_S} + g k_{\text{B}} T \ln S \end{aligned} \tag{12}$$

The equations of motion for the extended system in *virtual* variables can now be derived in the canonical way from the hamiltonian. First the equations of motion for the atomic *virtual* coordinates and momenta in terms of derivatives of the *virtual* time coordinate can be written

$$\begin{aligned} \frac{\mathrm{d}\vec{\pi}_i}{\mathrm{d}\tau} &= -\frac{\partial \mathcal{H}}{\partial \vec{\rho}_i} = -Q^{1/3} \frac{\partial \mathcal{V}(\{\vec{\rho} Q^{1/3}\})}{\partial (\vec{\rho}_i Q^{1/3})} = Q^{1/3} \vec{F}_i \\ \frac{\mathrm{d}\vec{\rho}_i}{\mathrm{d}\tau} &= \frac{\partial \mathcal{H}}{\partial \vec{\pi}_i} = \frac{\vec{\pi}_i}{m_i S^2 Q^{2/3}} \end{aligned} \tag{13}$$

where $\vec{F}_i$ is the total force on atom i

$$\vec{F}_i = -\frac{\partial \mathcal{V}(\{\vec{r}_1, \vec{r}_2, \ldots, \vec{r}_N\})}{\partial \vec{r}_i}. \tag{14}$$

The equations of motion for Q and its conjugate momentum are

$$\begin{aligned} \frac{\mathrm{d}\Pi_Q}{\mathrm{d}\tau} &= -\frac{\partial \mathcal{H}}{\partial Q} = \frac{1}{3Q} \sum_{i=1}^{N} \left[\frac{\vec{\pi}_i \cdot \vec{\pi}_i}{m_i S^2 Q^{2/3}} + Q^{1/3} \vec{F}_i \cdot \vec{\rho}_i \right] - P_{\text{ext}} \\ \frac{\mathrm{d}Q}{\mathrm{d}\tau} &= \frac{\partial \mathcal{H}}{\partial \Pi_Q} = \frac{\Pi_Q}{M_Q S^2} \end{aligned} \tag{15}$$

and the equations of motion for S and its conjugate momentum are

$$\begin{aligned}
\frac{\mathrm{d}\Pi_S}{\mathrm{d}\tau} &= -\frac{\partial \mathcal{H}}{\partial S} = \sum_{i=1}^{N} \frac{\vec{\pi}_i \cdot \vec{\pi}_i}{m_i S^3 Q^{2/3}} + \frac{\Pi_Q^2}{M_Q S^3} - \frac{g k_{\mathrm{B}} T}{S} \\
\frac{\mathrm{d}S}{\mathrm{d}\tau} &= \frac{\partial \mathcal{H}}{\partial \Pi_S} = \frac{\Pi_S}{M_S}.
\end{aligned} \tag{16}$$

Equations of motion in real space

These equations of motion could be solved numerically to produce a time trajectory in the *virtual* phase space of the extended system. However this turns out not to be the best choice as integrating with a constant time step $\Delta\tau$ over the *virtual* time implies producing a trajectory unevenly spaced in the *real* time of the system of interest. It is therefore more rewarding to go back from the coordinates and momenta in *virtual* space $\{\vec{\rho}^N, \vec{\pi}^N, Q, \Pi_Q, S, \Pi_S; \tau\}$ to the coordinates and momenta in *real* space $\{\vec{r}^N, \vec{p}^N, V, P_V, s, P_s; t\}$ by means of the following transform relations

$$\begin{array}{llll}
\vec{r}_i = \vec{\rho}_i Q^{-1/3} & V = Q & s = S & \\
\vec{p}_i = \vec{\pi}_i / S Q^{1/3} & P_V = \Pi_Q / S & P_s = \Pi_S & \mathrm{d}t = \mathrm{d}\tau / s.
\end{array} \tag{17}$$

The equations of motion become

$$\begin{aligned}
\dot{\vec{r}}_i &= \frac{\vec{p}_i}{m_i} + \vec{r}_i \frac{\dot{V}}{3V} \\
\dot{\vec{p}}_i &= \vec{F}_i - \vec{p}_i \frac{\dot{s}}{s} - \vec{p}_i \frac{\dot{V}}{3V} \\
\dot{V} &= \frac{P_V}{M_Q} \\
\dot{P}_V &= \frac{1}{3V} \sum_{i=1}^{N} \left[\frac{\vec{p}_i^{\,2}}{m_i} + \vec{F}_i \cdot \vec{r}_i \right] - P_{\mathrm{ext}} - P_V \frac{\dot{s}}{s} \\
\dot{s} &= s \frac{P_s}{M_S} \\
\dot{P}_s &= \sum_{i=1}^{N} \left[\frac{\vec{p}_i^{\,2}}{m_i} \right] + \frac{P_V^2}{M_Q} - g k_{\mathrm{B}} T
\end{aligned} \tag{18}$$

where the dot stands for the time derivative with respect to t.

The Hamiltonian $\mathcal{H}$ in eqn (12) can also be transformed, but it must be noticed that because the transformation is not canonical, the function

$$\mathcal{H} = \mathcal{K}(\vec{p}^N) + \mathcal{V}(\vec{r}^N) + \frac{P_V^2}{2M_Q} + P_{\text{ext}}V + \frac{P_s^2}{2M_S} + gk_{\text{B}}T\ln s \tag{19}$$

obtained cannot be used to derive hamiltonian equations of motion for the *real* coordinates and momenta $\{\vec{r}^N, \vec{p}^N, V, P_V, s, P_s; t\}$, while it still remains a constant of motion for the time evolution defined by eqns (18).

Time and ensemble averages

Solving numerically eqns (18), one can produce a time trajectory for the extended system and therefore calculate time averages as in the standard molecular dynamics to estimate the macroscopic properties of the system of interest. We must ask ourselves what kind of averages are we calculating with respect to statistical mechanics ensembles. We know that our time trajectory corresponds, by invoking the ergodic hypothesis, to a microcanonical ensemble distribution for the extended system in the *virtual phase space*. We are, however, interested in the properties of the system of interest which can be quite generally expressed as ensemble averages of an observable $\mathcal{F}(\vec{r}^N, \vec{p}^N, V; t)$ The corresponding observable $\mathcal{G}$ in the *virtual space* is defined as

$$\begin{aligned} \mathcal{F}(\vec{r}^N, \vec{p}^N, V; t) &\equiv \mathcal{F}(Q^{1/3}\vec{\rho}^N, S^{-1}Q^{-1/3}\vec{\pi}^N, S, Q; \tau), \quad \tau = \tau(t) \\ &= \mathcal{G}(\vec{\rho}^N, \vec{\pi}^N, Q, \Pi_Q, S, \Pi_S; \tau). \end{aligned} \tag{20}$$

What can be readily calculated from the dynamical trajectory is a time average of the form

$$\langle\mathcal{F}\rangle_t = \lim_{t_l\to\infty} \frac{\int_0^{t_l} \mathrm{d}t \; \mathcal{F}(\vec{r}^N(t), \vec{p}^N(t), V(t))}{\int_0^{t_l} \mathrm{d}t} \tag{21}$$

which then corresponds to an average over the *virtual time* τ

$$= \lim_{\tau_l(t_l)\to\infty} \frac{\int_0^{\tau_l} \mathrm{d}\tau \; \mathcal{G}(\vec{\rho}^N, \vec{\pi}^N, Q, \Pi_Q, S, \Pi_S; \tau)/S(\tau)}{\int_0^{\tau_l} \mathrm{d}\tau \; 1/S(\tau)} = \frac{\langle\mathcal{G}/S\rangle_\tau}{\langle 1/S\rangle_\tau}. \tag{22}$$

The above equation sets the equivalence between the dynamical averages in the two pictures of *virtual* and *real* time. But we know that, if the motion of the system is ergodic, time averages over τ are equivalent to microcanonical ensemble averages

$$\frac{\langle \mathcal{G}/S\rangle_\tau}{\langle 1/S\rangle_\tau} \Leftrightarrow \frac{\langle \mathcal{G}/S\rangle_{\rm mc}}{\langle 1/S\rangle_{\rm mc}} = \langle \mathcal{F}\rangle_{\rm Ensemble?} \tag{23}$$

which can be made more explicit

$$\begin{aligned} \frac{\langle \mathcal{G}/S\rangle_{\rm mc}}{\langle 1/S\rangle_{\rm mc}} &= \left\{\frac{\int \mathrm{d}\mathbf{\Omega}\ [1/S]\delta(\mathcal{H}-E)}{\int \mathrm{d}\mathbf{\Omega}\ \delta(\mathcal{H}-E)}\right\}^{-1} \\ &\quad \times \frac{\int \mathrm{d}\mathbf{\Omega}\ [\mathcal{G}(\vec{\rho}^N, \vec{\pi}^N, Q, \Pi_Q, S, \Pi_S)/S)]\delta(\mathcal{H}-E)}{\int \mathrm{d}\mathbf{\Omega}\ \delta(\mathcal{H}-E)} \\ &= \frac{\int \mathrm{d}\mathbf{\Omega}\ [\mathcal{G}(\vec{\rho}^N, \vec{\pi}^N, Q, \Pi_Q, S, \Pi_S)/S]\delta(\mathcal{H}-E)}{\int \mathrm{d}\mathbf{\Omega}\ [1/S]\delta(\mathcal{H}-E)}. \end{aligned} \tag{24}$$

Here we introduced a short notation for the integration variables $\mathrm{d}\mathbf{\Omega}$ in the *virtual* phase space. The transformation relating it to the *real* phase space integration variables $\mathrm{d}\mathbf{\Gamma}$ is characterised by a jacobian which is readily calculated

$$\begin{aligned} \int \mathrm{d}\mathbf{\Omega} &= \int \mathrm{d}\vec{\rho}^N \mathrm{d}\vec{\pi}^N \mathrm{d}Q \mathrm{d}\Pi_Q \mathrm{d}S \mathrm{d}\Pi_S \\ &= \int \mathrm{d}\vec{r}^N \mathrm{d}\vec{p}^N \mathrm{d}V \mathrm{d}P_V \mathrm{d}s \mathrm{d}P_s\ s^{3N+1} = \int \mathrm{d}\mathbf{\Gamma}\ s^{3N+1}. \end{aligned} \tag{25}$$

What we have to do is now to find out to which ensemble the *real* time average

$$\langle \mathcal{F}\rangle_t \Leftrightarrow \langle \mathcal{F}\rangle_{\rm Ensemble?} = \frac{\int \mathrm{d}\mathbf{\Omega}\ [\mathcal{G}(\vec{\rho}^N, \vec{\pi}^N, Q, \Pi_Q, S, \Pi_S)/S]\delta(\mathcal{H}-E)}{\int \mathrm{d}\mathbf{\Omega}\ [1/S]\delta(\mathcal{H}-E)} \tag{26}$$

corresponds, in the ergodic limit. To do this we have to transform the integrals in the above equations into integrals over the space $\{\vec{r}^N, \vec{p}^N, V\}$ and perform the integral over the extra reservoir variables. Having already expressed the required jacobian we must make explicit the transformation of the microcanonical delta function distribution $\delta(\mathcal{H}-E)$. We first observe that

$$\delta(f(s)) = \delta(s-s_0)/f'(s_0) \qquad f'(s_0) = gk_{\rm B}T/s_0. \tag{27}$$

Here we should really have a sum over all possible zeroes of f, but in this case we can state that there is only one zero at

$$s_0 = \exp\{-(\mathcal{H}_T - E)/gk_{\rm B}T\} \tag{28}$$

because the dependence on s is logarithmic. It is useful at this time to introduce the function $\mathcal{H}_T$

$$\mathcal{H}_T = \sum_{i=1}^{N} \frac{\vec{p}_i^{\,2}}{2m_i} + \mathcal{V}(\vec{r}^N) + \frac{P_V^2}{2M_Q} + P_{\mathrm{ext}}V + \frac{P_s^2}{2M_S} \tag{29}$$

in terms of which the microcanonical delta function

$$\delta(\mathcal{H}(\vec{r}^N, \vec{p}^N, V, P_V, s, P_s) - E) \tag{30}$$

can be reformulated in a compact way

$$\frac{1}{gk_{\mathrm{B}}T} \exp\{-(\mathcal{H}_T - E)/gk_{\mathrm{B}}T\}\delta(s - s_0). \tag{31}$$

We can now write for the denominator in eqn (24)

$$\int \mathrm{d}\boldsymbol{\Omega}\; [1/S]\delta(\mathcal{H} - E) = \int \mathrm{d}\boldsymbol{\Gamma}\; [s^{3N+1}]\, \frac{s_0}{gk_{\mathrm{B}}T}(1/s)\delta(s - s_0) \tag{32}$$

which after the integration over the variable s has been performed becomes

$$= \frac{1}{gk_{\mathrm{B}}T} \int \mathrm{d}\vec{r}^N \mathrm{d}\vec{p}^N \mathrm{d}V \mathrm{d}P_V \mathrm{d}P_s\; \exp\left\{-\left(\frac{3N+1}{g}\right)\frac{\mathcal{H}_T - E}{k_{\mathrm{B}}T}\right\}. \tag{33}$$

Equivalently we can dispose of the numerator which becomes

$$\int \mathrm{d}\boldsymbol{\Omega}\; [\mathcal{G}/S]\delta(\mathcal{H} - E) =$$
$$\frac{1}{gk_{\mathrm{B}}T} \int \mathrm{d}\vec{r}^N \mathrm{d}\vec{p}^N \mathrm{d}V \mathrm{d}P_V \mathrm{d}P_s\; \mathcal{F} \exp\left\{-\left(\frac{3N+1}{g}\right)\frac{\mathcal{H}_T - E}{k_{\mathrm{B}}T}\right\}. \tag{34}$$

We can now fix the number of degrees of freedom g. By choosing $g = 3N + 1$ we can finally write

$$\langle \mathcal{F} \rangle_{\mathrm{Ensemble?}} = \frac{\int \mathrm{d}\vec{r}^N \mathrm{d}\vec{p}^N \mathrm{d}V \mathrm{d}P_V \mathrm{d}P_s\; \mathcal{F} \exp\{-\mathcal{H}_T/k_{\mathrm{B}}T\}}{\int \mathrm{d}\vec{r}^N \mathrm{d}\vec{p}^N \mathrm{d}V \mathrm{d}P_V \mathrm{d}P_s\; \exp\{-\mathcal{H}_T/k_{\mathrm{B}}T\}} \tag{35}$$

which can be further simplified observing that the observable $\mathcal{F}$ does not depend on the momenta P_V, P_s. After integration over these variables the constant temperature - constant pressure NPT ensemble average is obtained

$$\langle \mathcal{F} \rangle_{NPT} =$$
$$\frac{\int \mathrm{d}\vec{r}^N \mathrm{d}\vec{p}^N \mathrm{d}V\; \mathcal{F}(\vec{r}^N, \vec{p}^N, V) \exp\left\{-[\mathcal{K}(\vec{p}^N) + \mathcal{V}(\vec{r}^N) + P_{\mathrm{ext}}V]/k_{\mathrm{B}}T\right\}}{\int \mathrm{d}\vec{r}^N \mathrm{d}\vec{p}^N \mathrm{d}V\; \exp\left\{-[\mathcal{K}(\vec{p}^N) + \mathcal{V}(\vec{r}^N) + P_{\mathrm{ext}}V]/k_{\mathrm{B}}T\right\}}. \tag{36}$$

Therefore we arrive at the conclusion that the time averages computed over the dynamical trajectory obtained by integrating eqns (18) numerically are equivalent, if the motion is ergodic, to the NPT ensemble averages

$$\langle \mathcal{F} \rangle_t \Leftrightarrow \langle \mathcal{F} \rangle_{NPT}. \tag{37}$$

Nosé-Hoover thermostat

In 1985 Hoover [3] reformulated Nosé equations for NVT simulations in a way which is considered simpler and easier for making further generalizations, as it avoids the need for introducing *virtual* variables. The Hoover procedure follows the demonstration used for the constraint methods [9]. Consider the distribution function $\varrho(\vec{r}^N, \vec{p}^N, \ldots)$ defined in the extended phase space $\mathbf{\Gamma} = \{\vec{r}^N, \vec{p}^N, \ldots\}$, where we leave undefined the extra variables for the moment. A generalised Liouville equation expresses the conservation of probability in this phase space,

$$\frac{\partial \varrho}{\partial t} + \frac{\partial}{\partial \mathbf{\Gamma}} \cdot (\dot{\mathbf{\Gamma}} \varrho) = 0. \tag{38}$$

The change of ϱ along a phase space trajectory is given by the total time derivative

$$\frac{\mathrm{d}\varrho}{\mathrm{d}t} = \frac{\partial \varrho}{\partial t} + \dot{\mathbf{\Gamma}} \cdot \frac{\partial}{\partial \mathbf{\Gamma}} \varrho. \tag{39}$$

When combined one obtains

$$\frac{\mathrm{d}\varrho}{\mathrm{d}t} = -\varrho \left(\frac{\partial}{\partial \mathbf{\Gamma}} \cdot \dot{\mathbf{\Gamma}} \right) \tag{40}$$

which in the case of hamiltonian dynamics equals zero and expresses Liouville's theorem. As we already said the equations of motion in *real* variables for the extended systems cannot be derived directly from a hamiltonian, and therefore we have to use eqn (40) to find the evolution of the distribution function ϱ. So the idea is to write down a set of equations of motion and then find out what they predict for the time dependence of the distribution function ϱ, by putting them in eqn (40).

Rather then simply repeating the demonstration for the case considered in section we shall write the equations for constant temperature - constant pressure simulation with a varying box shape, following the generalisation of the Andersen method due to Parrinello and Rahman[7]. In this case the volume variable is replaced by the 3×3 matrix variable $\overleftrightarrow{h}$, shorthand for the three lattice vectors $(\vec{a}, \vec{b}, \vec{c})$ which describe the shape and volume of the MD box and, as a consequence, the periodic boundary conditions in a Bravais lattice notation.

It has been pointed out [10] that only six of these nine variables have an interesting meaning, when the three degrees of freedom describing the overall rotation of the MD box are extracted out. The situation is very simple in atomic cases where one can show that the equations of motion conserve symmetric matrices $\overleftrightarrow{h}$. This is no longer true for the case of molecular systems, when intramolecular distances are kept fixed and the coupling is via the molecular centres of mass. In order to avoid overall rotation of the MD box, which, especially for solids, would simply confuse the analysis of the trajectories of the system, two options have been used both of which reduce the number of extra variables to six. In one case [10] the matrix $\overleftrightarrow{h}$ is kept symmetric by disregarding the asymmetric contributions in the equations of motion, and in the other one [11] the variables are reduced to six by fixing the MD box orientation with respect to a *laboratory* frame, and specifically by choosing $\vec{a}$ parallel to the x-axis and $\vec{b}$ to lie in the xy plane. This choice results in an upper triangular matrix $\overleftrightarrow{h}$. Also it is possible to make other choices (for example only allowing fluctuations of the box which maintain a parallelepiped shape, which makes 3 degrees of freedom and the matrix is diagonal), therefore we shall generally leave undefined the number of degrees of freedom of the box, and will indicate them by g_h. When using the Parrinello-Rahman technique, special care must be taken in the application of periodic boundary conditions as will be clarified later on.

Let's start by writing down the new equations of motions for the set of variables $\mathbf{\Gamma} = \{\vec{r}^N, \vec{p}^N, \overleftrightarrow{h}, \overleftrightarrow{P}_h, \zeta\}$

$$
\begin{aligned}
\dot{\vec{r}}_i &= \frac{\vec{p}_i}{m_i} + \left[\overleftrightarrow{h}^{-1} \dot{\overleftrightarrow{h}}\right] \vec{r}_i \\
\dot{\vec{p}}_i &= \vec{F}_i - \zeta \vec{p}_i - \left[\overleftrightarrow{h}^{-1} \dot{\overleftrightarrow{h}}\right] \vec{p}_i \\
\left[\dot{\overleftrightarrow{P}}_h\right]_{xy} &= \sum_{z=1}^{3} \left[\overleftrightarrow{h}^{-1}\right]_{zx} \left[\sum_{i=1}^{N} \frac{\vec{p}_i \vec{p}_i}{m_i} + \vec{F}_i \vec{r}_i\right]_{zy} - \left[\overleftrightarrow{h}^{-1}\right]_{yx} P_{\mathrm{ext}} \det \overleftrightarrow{h} - \zeta \left[\overleftrightarrow{P}_h\right]_{xy} \\
\dot{\zeta} &= \frac{1}{M_S} \left\{ \sum_{i=1}^{N} \frac{\vec{p}_i^{\,2}}{m_i} + \sum_{x,y=1}^{3} \frac{1}{M_Q} \left[\overleftrightarrow{P}_h^{2}\right]_{xy} - g k_{\mathrm{B}} T \right\} \qquad (41)
\end{aligned}
$$

$$\left[\dot{\overleftrightarrow{h}}\right]_{xy} = \frac{1}{M_Q}\left[\overleftrightarrow{P}_h\right]_{xy}$$

where, following Hoover, the role of the Nosé coordinate s and the momentum P_s is played by the single coordinate ζ which is related to them by

$$\zeta = \frac{\mathrm{d}\ln s}{\mathrm{d}t} = \frac{\dot{s}}{s} = \frac{P_s}{M_S}. \tag{42}$$

The equations of motion do not depend on the variable s explicitly, but s appears when we consider the constant of the motion $\mathcal{H}$

$$\mathcal{H} = \mathcal{H}_T + gk_{\mathrm{B}}T\ln s \tag{43}$$

where $\mathcal{H}_T$ has been defined as

$$\mathcal{H}_T = \sum_{i=1}^{N}\frac{\vec{p}_i^{\,2}}{2m_i} + \mathcal{V}(\vec{r}^{\,N}) + \sum_{x,y=1}^{3}\frac{1}{2M_Q}\left[\overleftrightarrow{P}_h^{\,2}\right]_{xy} + P_{\mathrm{ext}}\det\overleftrightarrow{h} + \frac{M_S\zeta^2}{2}. \tag{44}$$

To demonstrate that $\mathcal{H}$ is indeed a conserved quantity let's first see what this requires for the time dependence of $\mathcal{H}_T$

$$\frac{\mathrm{d}\mathcal{H}}{\mathrm{d}t} = 0 \Leftrightarrow \frac{\mathrm{d}\mathcal{H}_T}{\mathrm{d}t} = -\frac{\mathrm{d}}{\mathrm{d}t}(gk_{\mathrm{B}}T\ln s) = -gk_{\mathrm{B}}T\zeta. \tag{45}$$

This can be readily verified

$$\begin{aligned}\frac{\mathrm{d}\mathcal{H}_T}{\mathrm{d}t} &= \sum_{i=1}^{N}\left\{\dot{\vec{p}}_i\cdot\frac{\partial\mathcal{H}_T}{\partial\vec{p}_i} + \dot{\vec{r}}_i\cdot\frac{\partial\mathcal{H}_T}{\partial\vec{r}_i}\right\} + \sum_{x,y=1}^{3}\left[\dot{\overleftrightarrow{P}}_h\right]_{xy}\frac{\partial\mathcal{H}_T}{\partial\left[\overleftrightarrow{P}_h\right]_{xy}} \\ &\quad + \sum_{x,y=1}^{3}\left[\dot{\overleftrightarrow{h}}\right]_{xy}\frac{\partial\mathcal{H}_T}{\partial\left[\overleftrightarrow{h}\right]_{xy}} + \dot{\zeta}\frac{\partial\mathcal{H}_T}{\partial\zeta} \\ &= -gk_{\mathrm{B}}T\zeta\,.\end{aligned} \tag{46}$$

The equation for the probability distribution can now be calculated

$$\begin{aligned}\frac{\mathrm{d}\varrho}{\mathrm{d}t} &= -\varrho\left(\frac{\partial}{\partial\mathbf{\Gamma}}\cdot\dot{\mathbf{\Gamma}}\right) \\ &= -\varrho\left\{\left[\sum_{i=1}^{N}\frac{\partial\dot{\vec{p}}_i}{\partial\vec{p}_i} + \frac{\partial\dot{\vec{r}}_i}{\partial\vec{r}_i}\right] + \frac{\partial\dot{\overleftrightarrow{P}}_h}{\partial\overleftrightarrow{P}_h} + \frac{\partial\dot{\overleftrightarrow{h}}}{\partial\overleftrightarrow{h}} + \frac{\partial\dot{\zeta}}{\partial\zeta}\right\} \\ &= \varrho(3N+g_h)\zeta = -\frac{1}{k_{\mathrm{B}}T}\frac{(3N+g_h)}{g}\frac{\mathrm{d}\mathcal{H}_T}{\mathrm{d}t}\varrho\end{aligned} \tag{47}$$

and this corresponds, by choosing $g = 3N + g_h$, to an equilibrium solution for ϱ of canonical form

$$\varrho \propto \exp\left\{-\frac{\mathcal{H}_T}{k_B T}\right\}. \tag{48}$$

Numerical considerations

A numerical problem arises specifically in the Parrinello-Rahman method. In this case the MD box has no longer a cubic shape and the algorithm to compute the minimum image in the presence of periodic boundary conditions has to be modified. The easiest possibility is to use virtual coordinates $\vec{\rho}_i$. In this space, in fact, the MD box is again a cube of unit size. Given a particle k, one has that each component ξ of the distance $\vec{d}_j^{(\xi)}$ computed as follows with any other particle j

$$\vec{d}_j^{(\xi)} = (\vec{\rho}_k^{(\xi)} - \vec{\rho}_j^{(\xi)}) - \mathtt{N}INT(\vec{\rho}_k^{(\xi)} - \vec{\rho}_j^{(\xi)}) \tag{49}$$

is, in absolute value, less than 0.5, that is the vector $\vec{d}_j^{(\xi)}$ selects the image of the particle j which is within the MD box centered at the position of particle k. This is sufficient to identify the minimum image with cubic periodic boundary conditions, but for the general triclinic case $|\vec{d}_j^{(\xi)}|$ can happen not to be the minimum distance between particle k and particle j and its images. The situation is clearly rendered in Fig. 1 where also it is shown that a more

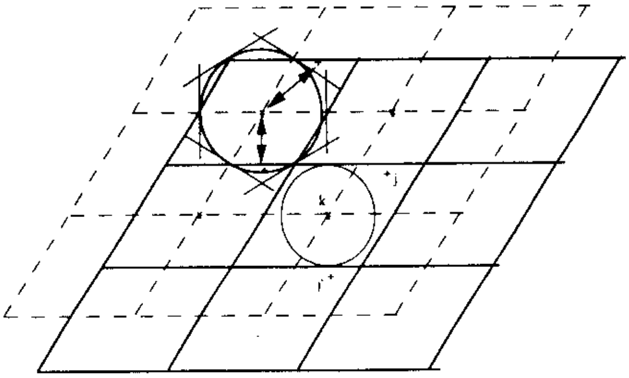


Figure 1: Minimum image convention in general triclinic periodic boundaries

general periodic boundary condition and minimum image convention could be used to solve this problem. However rather than getting involved in such a complexity it can be immediately seen that eqn (49) still defines the minimum image for vectors $\vec{d}_j^{(\xi)}$ which, in *real* space, are inside the largest sphere inscribable in the triclinic box, that is for distances $|\vec{d}_j^{(\xi)}|$ less than half the minimum of the three distances between the faces of the triclinic box. These can be easily computed dividing the volume of the box by the area of the faces, or more simply as the inverse of the reciprocal lattice vectors.

A few words of caution are to be devoted to the evaluation of the pressure tensor, particularly in molecular systems. The molecular expressions cannot be evaluated as such when periodic boundary conditions are applied to the system. The force $\mathbf{F}_j$ on atom j is the sum of several other pair contributions $\mathbf{F}_{jk}$, and eventually of many-body terms, which are computed with the minimum image convention. This implies that the identity of the atomic positions $\mathbf{r}_j$ to be used in the evaluation of the virial sum changes from pair to pair. It is well known, although not well documented, that in the simple case of pair-only interactions this problem can be readily overcome. The virial sum over the atomic index j can be transformed into a sum over pairs

$$\sum_j \mathbf{r}_j \mathbf{F}_j = \sum_{j>k} (\mathbf{r}_j - \mathbf{r}_k) \mathbf{F}_{jk} \tag{50}$$

where now the interaction forces $\mathbf{F}_{jk}$ and distances $(\mathbf{r}_j - \mathbf{r}_k)$ are consistently referred to the same minimum image pair. When dealing with molecules the situation becomes, of course, more complex. First there are two possible ways of implementing the minimum image convention. One way is to consider molecules as 'indivisible' and therefore search for minimum images molecule by molecule, usually with reference to the molecular center of mass. The other possibility is to continue to consider each interaction site individually and proceed as for atomic systems. In the former case the molecular virial can be calculated as in eqn (50), replacing atomic quantities with the corresponding molecular ones.

However, even if the difference between the two approaches is usually small, being restricted to interactions close to the cut-off distance, there are cases in which it is more sensible to use the latter approach. Large molecules with internal degrees of freedom, where the center of mass changes with time its relative position to constituent atoms, and systems with long-range forces are examples of these. In such a case special attention has to be paid when evaluating the pressure tensor. For simplicity let us consider only the interaction term for one component, say xz, of the *molecular* pressure tensor

$$T^{xz} = \sum_{\alpha=1}^{N} x_\alpha F_\alpha^z \tag{51}$$

for the case of pair interactions only. When the sum over pairs is made explicit one has

$$\begin{aligned} T^{xz} &= \sum_{\alpha=1}^{N}\sum_{i=1}^{n} x_\alpha F_{i\alpha}^z = \sum_{\alpha=1}^{N}\sum_{i=1}^{n} x_\alpha \sum_{\alpha\neq\beta=1}^{N}\sum_{j=1}^{n} F_{i\alpha j\beta}^z \\ &= \sum_{\alpha\neq\beta=1}^{N}\sum_{i,j=1}^{n} x_\alpha F_{i\alpha j\beta}^z = \sum_{\alpha,\beta>\alpha=1}^{N}\sum_{i,j=1}^{n} (x_\alpha - x_\beta) F_{i\alpha j\beta}^z \end{aligned} \tag{52}$$

where use has been made of the equality

$$F_{i\alpha j\beta}^z = -F_{j\beta i\alpha}^z. \tag{53}$$

Equation (52) can be reorganized after adding and subtracting terms $(x_{i\alpha} - x_{j\beta})$

$$\begin{aligned} T^{xz} &= \sum_{\alpha,\beta>\alpha=1}^{N}\sum_{i,j=1}^{n} (x_{i\alpha} - x_{j\beta}) F_{i\alpha j\beta}^z \\ &+ \sum_{\alpha,\beta>\alpha=1}^{N}\sum_{i,j=1}^{n} [(x_\alpha - x_{i\alpha}) - (x_\beta - x_{j\beta})] F_{i\alpha j\beta}^z \end{aligned} \tag{54}$$

and finally we obtain

$$T^{xz} = \sum_{\alpha,\beta>\alpha=1}^{N}\sum_{i,j=1}^{n} (x_{i\alpha} - x_{j\beta}) F_{i\alpha j\beta}^z - \sum_{\alpha=1}^{N}\sum_{i=1}^{n} (x_{i\alpha} - x_\alpha) \sum_{\beta\neq\alpha=1}^{N}\sum_{j=1}^{n} F_{i\alpha j\beta}^z. \tag{55}$$

It is now possible to distinguish two terms which can be evaluated in a non-ambiguous way in the presence of periodic boundary conditions. The first term is simply the *atomic* term, where however only intermolecular interactions do appear, and the second term represents the correction needed to obtain the *molecular* property. It has to be stressed that in this representation intramolecular interactions, arising either from constraint forces or from potential terms, do not need to be considered explicitly for the calculation of the pressure, as their contribution to the total force on the molecule vanishes.

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MD simulation of rare events: Calculation of rate constants

An activated process is a transition between stable states, i.e. states where the system spends the overwhelming majority of its time, separated by a region of low probability and can be viewed as the crossing of a free energy barrier. When the free energy barrier is much higher than k_BT the crossing is an infrequent event often of short duration which cannot be simulated using conventional techniques. If the activated process can be described by a phenomenological rate equation, then the associated rate constants can be calculated within the reactive-flux correlation function formalism[1, 2].

Classically transitions between stable states in a many-body dynamical system can be often described by a suitable function of the configuration space called the reaction coordinate or progress variable, denoted by $\xi(\mathbf{r})$, where $\mathbf{r}$ represents the set of coordinates of all the degrees of freedom of the system. The progress variable ξ can be thought of as a collective variable whose values describe the state of advancement of the reaction when going from one stable state to the other. The probability density to find the system in any point of the configuration space such that $\xi(\mathbf{r})$ equals a prescribed value ξ' is :

$$P(\xi = \xi') = \left\langle \delta(\xi(\mathbf{r}) - \xi') \right\rangle \equiv C e^{-\beta W(\xi')} \tag{1}$$

where $< \ldots >$ is the canonical ensemble average, $\beta = \frac{1}{k_BT}$ and the last equality is a definition of the potential of mean force $W(\xi)$ associated with the reaction coordinate. $W(\xi_1) - W(\xi_2)$ expresses the reversible work needed to take the system from some reference value ξ_2 of the variable ξ to ξ_1. The constant C is determined by the normalization condition on $P(\xi)$. If $\xi^\dagger$ is a local maximum for $W(\xi)$ we can identify the hyper-surface $\xi(\mathbf{r}) = \xi^\dagger$ as the transition region and $P(\xi^\dagger)$ is one of the important quantities we wish to calculate. Of course special methods have to be used to determine the probability of a highly improbable value of ξ. They include special sampling schemes; for example, umbrella sampling[3], to compute mean force potential differences $W(\xi') - W(\xi)$ or the mean force on ξ , $F(\xi) = -\frac{dW(\xi)}{d\xi}$. The rate constant in turn can be computed, knowing this probability, as the product of the $P(\xi^\dagger)$ and the average fraction of trajectories which, starting at the transition point $\xi^\dagger$, end in the product region. The classical treatment of chemical reactions we have just described was first introduced by Keck[4, 5] and Anderson[6] to treat gas phase chemical reactions and later applied by Bennett[7, 8] and Chandler[1] to the treatment of condensed-phase rate processes.

Reactive Flux Correlation Formulas

We begin this section by recalling the autocorrelation function expressions for the rate constant of a reaction. These expressions were first derived by Yamamoto[9] in 1960 and have continued to fascinate researchers in the area as is evidenced by the number of times they have been re-derived and reinterpreted in the literature[2, 10, 11, 12, 13].

In order to give a statistical mechanical definition of the rate of the reaction

$$A \rightleftharpoons B \, , \tag{2}$$

we must first introduce a microscopic definition of the chemical species A and B. This is achieved by using the progress variable ξ and defining the states corresponding to species A as those such that $\xi < \xi^\dagger$ while the complementary range defines species B. The dividing surface between the two species, $\xi = \xi^\dagger$, identifies the rarest value of ξ which must be crossed when trasforming A to B (or vice versa). The microscopic variable

$$\hat{n}_A(\xi) = \theta(\xi^\dagger - \xi(\mathbf{r})) = \begin{cases} 1 & \xi < \xi^\dagger \\ 0 & \xi > \xi^\dagger \end{cases} \tag{3}$$

characterizes microscopically the species A ($n_A =< \hat{n}_A >$, as usual) while

$$\dot{\hat{n}}_A(\xi) = -\dot{\xi}\delta(\xi^\dagger - \xi) \tag{4}$$

is the microscopic expression for its flux.

If a phenomenological law is valid, one can write down a rate equation for the reaction and identify the forward and reverse rate coefficient, k_f and k_r respectively.

By applying the fluctuation-dissipation theorem one finds that the rate coefficient, say k_f, can be computed in microscopic terms from the plateau value of the quantity $k_f(t)$ defined by [9, 14]

$$\begin{aligned} k_f(t) &= \frac{1}{n_A}\int_0^t < \dot{\hat{n}}_A(\xi)\dot{\hat{n}}_A(\xi(t')) > dt' \\ &\equiv -\frac{1}{n_A} < \dot{\xi}\delta(\xi - \xi^\dagger)\theta(\xi^\dagger - \xi(t)) > \ . \end{aligned} \tag{5}$$

The limit $t \to 0_+$ of Eq. (5) plays a special role in the theory since it gives the transition state theory value for the rate constant[14]

$$k_f^{TST} = -\frac{1}{n_A} < \dot{\xi}\theta(-\dot{\xi})\delta(\xi - \xi^\dagger) >= \frac{1}{n_A} < \dot{\xi}\theta(\dot{\xi})\delta(\xi - \xi^\dagger) > , \tag{6}$$

where the last equality follows by time reversal invariance and k_f^{TST} is the reference value for most elementary treatments of the rate constant.

Finally, using the transition state theory expression, we may write the time dependent rate constant $k_f(t)$ in terms of the time dependent transmission coefficient $\kappa(t)$ as

$$k_f(t) = k^{TST}\kappa(t) , \tag{7}$$

which measures deviations due to dynamical effects associated with re-crossings of the species dividing surface.

Alternatively we can separate the static and dynamic contributions to the rate constant by multiplying and dividing the right hand side of Eq. (5) by $\langle\delta(\xi - \xi^\dagger)\rangle$. We then obtain

$$k_f(t) = (\frac{1}{n_A^{eq}} + \frac{1}{n_B^{eq}}) \left[\frac{\langle\dot{\xi}\delta(\xi - \xi^\dagger)\theta(\xi(t) - \xi^\dagger)\rangle}{\langle\delta(\xi - \xi^\dagger)\rangle}\right] \langle\delta(\xi - \xi^\dagger)\rangle . \tag{8}$$

The last term on the right hand side is the probability density to find the system at the transition state while the ratio in the square brackets is a conditional average, namely the average of the product $\dot{\xi}\theta(\xi(t) - \xi^\dagger)$ given that $\xi = \xi^\dagger$.

Blue Moon Ensemble

By simulation it is difficult to determine properties that depend on rare events. In the particular case of rare but fast events it is possible to circumvent the difficulty. For example to estimate the transition rate a computationally efficient way is to choose initial states localized at the hyper-surface that separates the stable regions. With such states one can compute the conditional average indicated in square brackets in Eq. (8). In addition one has to compute the equilibrium probability density for the system to be at the transition state.

Assuming that the activated process is described by the reaction coordinate $\xi(\mathbf{r})$, where $\mathbf{r} = (\mathbf{r_1}, \mathbf{r_2}, \ldots, \mathbf{r_N})$ represents the $3N$ Cartesian coordinates of the system composed of N particles with masses m_i ($i = 1, \ldots, N$) and, for simplicity, without internal structure, we want to compute ensemble averages of static or time dependent dynamical variables containing a delta function that localizes the system initially at a prescribed (rare) value of $\xi(\mathbf{r}) = \xi'$. The generalization to the case of molecules is straightforward unless constraints are used to freeze some of the intramolecular degrees of freedom[15].

The presence of the delta function is suggestive of the ensemble which describes our system when the reaction coordinate is constrained to the value prescribed by the delta function. To see the analogy let us derive the statistical mechanics in Cartesian coordinates of a system subjected to a holonomic constraint. Usually when there are constraints one introduces a set of generalized coordinates $\mathbf{q}$ and conjugate momenta $\mathbf{p}^q$ such that $\mathbf{r} = \mathbf{r}(\mathbf{q})$. In general it is not possible to invert this relation since there are more $\mathbf{r}$ coordinates than $\mathbf{q}$ coordinates. However by including the expression(s) for the constraint(s) one has extra generalized coordinate(s) and one recovers the one-to-one correspondence $\mathbf{r} = \mathbf{r}(\mathbf{q}, \textit{constraint expression(s)})$.

The statistical mechanics is easily formulated in terms of the generalized coordinates $\mathbf{q}$. However it may be useful to have the equivalent formulation of the statistical mechanics in terms of the original Cartesian coordinates. We now derive this expression for our N-particle system subjected to the holonomic constraint $\sigma(\mathbf{r}) = \xi(\mathbf{r}) - \xi' = 0$. The dynamics of the system is described in Cartesian coordinates by the Lagrangian

$$\mathcal{L}(\mathbf{r}, \dot{\mathbf{r}}) = K(\dot{\mathbf{r}}) - V(\mathbf{r}) = \sum_{i=1}^{N} \frac{1}{2} m_i \dot{\mathbf{r}}_i^2 - V(\mathbf{r}) \ , \tag{9}$$

to which we add the constraint $\sigma = 0$. The corresponding equations of motion are the Lagrange equations of first kind[16]. The set of $3N - 1$ generalized coordinates $\mathbf{q}$ plus σ can be taken as a new set of equivalent $3N$ coordinates denoted collectively by $\mathbf{u}$. We have

$$\mathbf{r} = \mathbf{r}(\mathbf{q}, \sigma) = \mathbf{r}(\mathbf{u}) \ , \tag{10}$$

or

$$\mathbf{u} = \mathbf{u}(\mathbf{r}) \ . \tag{11}$$

In the new variables the Lagrangian is given by

$$\mathcal{L}'(\mathbf{u}, \dot{\mathbf{u}}) = \frac{1}{2} \dot{\mathbf{u}}^T \mathbf{M} \dot{\mathbf{u}} - V'(\mathbf{u}) \ , \tag{12}$$

where $\mathbf{u}^T$ is the transpose of vector $\mathbf{u}$ and $\mathbf{M}$ is the metric matrix with elements given by

$$M_{\mu\nu} = \sum_{i=1}^{N} m_i \frac{\partial \mathbf{r}_i}{\partial u_\mu} \cdot \frac{\partial \mathbf{r}_i}{\partial u_\nu} \ . \tag{13}$$

The Lagrangian of the constrained motion is easily obtained by putting $\sigma = \dot{\sigma} = 0$, i.e.

$$\mathcal{L}_c(\mathbf{q}, \dot{\mathbf{q}}) \equiv \mathcal{L}'\left(\mathbf{q}, \sigma = 0, \dot{\mathbf{q}}, \dot{\sigma} = 0\right) \ . \tag{14}$$

To derive the statistical mechanical ensemble we need the Hamiltonian description of the dynamical system. The Hamiltonian in $\mathbf{u}$ coordinates is given by

$$\mathcal{H}'(\mathbf{u}, \mathbf{p}^u) = \frac{1}{2}\mathbf{p}^{uT}\mathbf{M}^{-1}\mathbf{p}^u + V'(\mathbf{u}) \ , \tag{15}$$

where

$$\mathbf{p}^u = \frac{\partial \mathcal{L}'}{\partial \dot{\mathbf{u}}} = \mathbf{M}\dot{\mathbf{u}} \ , \tag{16}$$

and the inverse of the metric matrix $\mathbf{M}^{-1}$ can be written explicitly as

$$(M^{-1})_{\mu\nu} = \sum_{i=1}^{N} \frac{1}{m_i} \frac{\partial u_\mu}{\partial \mathbf{r}_i} \cdot \frac{\partial u_\nu}{\partial \mathbf{r}_i} \ . \tag{17}$$

To obtain the constrained motion we have to compute the Hamiltonian at $\sigma = 0$ and p^σ satisfying the constraints $\sigma = \dot{\sigma} = 0$. Since

$$\dot{\sigma} = \left(\mathbf{M}^{-1}\mathbf{p}^u\right)_{3N} \equiv \mathbf{E}\mathbf{p}^q + Zp^\sigma \ , \tag{18}$$

where $\mathbf{E}$ and Z are suitable submatrices of $\mathbf{M}^{-1}$, the condition $\dot{\sigma} = 0$ yields $p^\sigma = -\tilde{Z}^{-1}\tilde{\mathbf{E}}\mathbf{p}^q$ where $\tilde{}$ means that the matrices have to be evaluated at $\sigma = 0$. Now we have for the constrained Hamiltonian

$$\mathcal{H}_c(\mathbf{q}, \mathbf{p}^q) \equiv \mathcal{H}'\left(\mathbf{q}, \sigma = 0, \mathbf{p}^q, p^\sigma = -\tilde{Z}^{-1}\tilde{\mathbf{E}}\mathbf{p}^q\right) \ . \tag{19}$$

Notice that Eq. (18) implies that

$$p^\sigma + Z^{-1}\mathbf{E}\mathbf{p}^q = Z^{-1}\dot{\sigma} \ . \tag{20}$$

Calling $\rho_\xi(\mathbf{q}, \mathbf{p}^q)$ the probability density corresponding to any possible ensemble for the constrained dynamical system, we have

$$\rho_c(\mathbf{q}, \mathbf{p}^q)\, d\mathbf{q}d\mathbf{p}^q \ = \ \rho'(\mathbf{u}, \mathbf{p}^u)\,\delta(\sigma)\delta(p^\sigma + Z^{-1}\mathbf{E}\mathbf{p}^q)d\mathbf{u}d\mathbf{p}^u$$

$$\begin{aligned} &= \rho(\mathbf{r},\mathbf{p}^r)\,\delta(\sigma)\delta(Z^{-1}\dot{\sigma})d\mathbf{r}d\mathbf{p}^r \\ &\equiv \rho_\xi(\mathbf{r},\mathbf{p}^r)\,d\mathbf{r}d\mathbf{p}^r\ , \end{aligned} \tag{21}$$

where in the second line of Eq. (21) we have used the fact that the variable transformation $(\mathbf{u},\mathbf{p}^u) \leftrightarrow (\mathbf{r},\mathbf{p}^r)$ is a canonical, volume conserving, transformation, since it is a point transformation[17].

For our purposes it is convenient to rewrite this probability as

$$\rho_\xi(\mathbf{r},\mathbf{p}^r) = \rho_\xi^r(\mathbf{r})\,\rho_\xi^p(\mathbf{p}^r|\mathbf{r})\ , \tag{22}$$

where the configurational probability density, $\rho_\xi^r(\mathbf{r})$, is obtained by performing the integration over momenta of the full probability density and the conditional probability density of the momenta given the configuration, $\rho_\xi^p(\mathbf{p}^r|\mathbf{r})$, is obtained by taking the ratio indicated in Eq. (22). To be more definite let us restrict our considerations to the canonical ensemble. Then the configurational probability density is given by

$$\rho_\xi^r(\mathbf{r})\,d\mathbf{r} = Q_c^{-1}|Z|^{\frac{1}{2}}exp[-\beta V(\mathbf{r})]\,\delta(\sigma)d\mathbf{r}\ , \tag{23}$$

where Q_c, the normalization factor, is the partition function of the constrained system and the conditional probability density of the momenta given the configuration is

$$\rho_\xi^p(\mathbf{p}^r|\mathbf{r})\,d\mathbf{p}^r = |Z|^{-\frac{1}{2}}exp[-\beta K]\,\delta(Z^{-1}\dot{\sigma})d\mathbf{p}^r\ , \tag{24}$$

where K is the kinetic energy and Z is defined by

$$Z = \sum_{i=1}^{N}\frac{1}{m_i}\frac{\partial\sigma}{\partial\mathbf{r}_i}\cdot\frac{\partial\sigma}{\partial\mathbf{r}_i}\ . \tag{25}$$

The physical meaning of the quantity Z has been discussed by several authors[18, 19, 20, 21] and has its origin in the restriction imposed in the momentum space by the validity of the constraint $\sigma = 0$ at all times which, in turn, requires that the generalized velocity $\dot{\sigma}$ vanishes at all times.

The probability densities we have been discussing up to now, more particularly the configurational probability density in Eq. (23), has to be compared with the configurational probability of the unconstrained system

$$\rho^r(\mathbf{r})\,d\mathbf{r} = Q^{-1}exp[-\beta V(\mathbf{r})]\,d\mathbf{r}\ , \tag{26}$$

or, even better, with the probability density to be at $\mathbf{r}$ and at $\xi = \xi'$

$$\rho^{r}(\mathbf{r})\,\delta(\xi(\mathbf{r}) - \xi')d\mathbf{r} = Q^{-1}exp[-\beta V(\mathbf{r})]\,\delta(\xi(\mathbf{r}) - \xi')d\mathbf{r}\,. \qquad (27)$$

At this stage we can take the essential step. Recall that, to improve statistics, we wish to express the conditional average of any configurational property of our system in terms of the ξ-constrained ensemble introduced above. Indeed, while by definition the value ξ' we want to sample is rare in the original ensemble, only configurations with $\xi = \xi'$ are sampled in the ξ-constrained ensemble. By simple inspection of Eq. (23) and Eq. (27) one finds that

$$\frac{< O(\mathbf{r})\delta(\xi(\mathbf{r}) - \xi') >}{< \delta(\xi(\mathbf{r}) - \xi') >} = \frac{< |Z|^{-1/2}O(\mathbf{r}) >_{\xi'}}{< |Z|^{-1/2} >_{\xi'}}\,, \qquad (28)$$

where the observable $O(\mathbf{r})$ is some function of the configuration space, $< \ldots >$ denotes the usual canonical average and $< \ldots >_{\xi'}$ denotes an average over the constrained ensemble with $\xi = \xi'$. Eq. (28) represents the fundamental result of the *Blue Moon* approach since it permits one to estimate the conditional average on the left hand side of this equation. This result was implicit in the work of Bennett[7] and Chandler[1] who did not use constraints but equivalent localizing procedures. To be useful Eq. (28) should be complemented with a numerically-workable procedure to compute $P_{\xi}(\xi') =< \delta(\xi - \xi') >$. To this end let us proceed as follows. Call $W(\xi') = -\frac{1}{\beta}ln\frac{P_{\xi}(\xi')}{C}$, where C is a normalization constant, the reversible work needed to bring the system from a given reference state to $\xi = \xi'$. The associated thermodynamic force

$$F(\xi') = -\frac{dW(\xi')}{d\xi'}\,, \qquad (29)$$

can be expressed as the conditional average of a suitable observable. Then, using Eq. (28) and a thermodynamic integration of $F(\xi')$ over ξ' we can obtain the desired probability.

To derive the explicit form of the thermodynamic force let us perform the derivative indicated in Eq. (29) with the help of a change of variables which introduces the Jacobian of the transformation, $|J|$. The result is

$$F(\xi') \;=\; \frac{1}{\beta}\frac{\frac{d}{d\xi'}\int d\mathbf{r}e^{-\beta V}\delta(\xi - \xi')}{\int d\mathbf{r}e^{-\beta V}\delta(\xi - \xi')}$$

$$
\begin{aligned}
&= \frac{1}{\beta}\frac{< \left(\frac{\partial}{\partial\xi} ln|J| - \beta\frac{\partial V}{\partial\xi}\right)\delta(\xi-\xi^{'}) >}{< \delta(\xi-\xi^{'}) >} \\
&\equiv \frac{< \hat{F}\delta(\xi-\xi^{'}) >}{< \delta(\xi-\xi^{'}) >} \ , \qquad (30)
\end{aligned}
$$

where $\hat{F}$ is composed of two terms, the first term $\frac{1}{\beta}\frac{\partial}{\partial\xi} ln|J|$ represents the apparent force acting on the system due to the use of generalized (non-inertial) coordinates, while the second term corresponds to the standard component of the force along the generalized coordinate ξ arising from the potential V.

The above result expresses the thermodynamic force as a conditional average; therefore it can be computed numerically by using the *Blue Moon* result, Eq. (28). To obtain this result we have proceeded as follows: Consider the numerator on the rhs of the first line of Eq. (30) and apply the transformation from the Cartesian coordinates **r** to the variables **u**. Performing the derivative and transforming back to the original coordinates one finds

$$
\begin{aligned}
\frac{d}{d\xi'}\int d\mathbf{r}e^{-\beta V}\delta(\xi-\xi^{'}) &= \int d\mathbf{q}d\xi\left[-\frac{\partial}{\partial\xi}\delta(\xi-\xi^{'})\right]|J|e^{-\beta V} \\
= \int d\mathbf{q}d\xi\delta(\xi-\xi^{'})\frac{\partial}{\partial\xi}\left[|J|e^{-\beta V}\right] &= \int d\mathbf{r}|J|^{-1}\delta(\xi-\xi^{'})\frac{\partial}{\partial\xi}\left[|J|e^{-\beta V}\right] \qquad (31)
\end{aligned}
$$

which gives the desired result.

There are two nasty quantities to be computed in Eq. (30), the Jacobian and the partial derivative with respect to ξ. Ruiz and Frenkel[22] have shown how to simplify this calculation by using as generalized coordinates **u** a set of orthogonal variables, i.e. a set such that

$$
\nabla u_\alpha \cdot \nabla u_\gamma = |\nabla u_\alpha|^2 \delta_{\alpha\gamma} \ , \qquad (32)
$$

where ∇ is the $3N$ dimensional vector given by the partial derivative with respect to the Cartesian coordinates of all particles **r**. Moreover, the coordinates **q** can be chosen so that $|\nabla q_\alpha| = 1$, $\alpha = 1, 3N-1$. Under these conditions it is easy to show that $|J| = |\nabla\xi|^{-1}$ and that

$$
\frac{\partial}{\partial\xi} = \frac{1}{|\nabla\xi|^2}(\nabla\xi)\cdot\nabla \ . \qquad (33)
$$

The constrained ensemble we have obtained can be generalized to give the biased configurational sample we already know and the correct distribution of momenta. This new *Blue Moon* ensemble can be easily obtained by multiplying the ξ-constrained configurational probability density by the correct (Maxwellian) conditional probability of the momenta.

$$\rho_{BM}(\mathbf{r},\mathbf{p}^r) = \rho^r_\xi(\mathbf{r})\rho^p(\mathbf{p}^r|\mathbf{r}) \; . \tag{34}$$

This ensemble provides a natural method for the computation of time correlation functions. What is required is to take an average over a *Blue Moon* ensemble of initial conditions of trajectories obtained by following the complete time evolution of the system after release of the constraint ξ (see Fig. 1). Hence given two arbitrary observables $O^{'}(\mathbf{r},\mathbf{p}^r)$ and $O^{''}(\mathbf{r},\mathbf{p}^r)$ we may write

$$\begin{aligned} & \frac{<O^{'}(\mathbf{r},\mathbf{p}^r)O^{''}(\mathbf{r}(t),\mathbf{p}^r(t))\delta(\xi(\mathbf{r})-\xi^{'})>}{<\delta(\xi(\mathbf{r})-\xi^{'})>} \\ = & \frac{<|Z|^{-1/2}O^{'}(\mathbf{r},\mathbf{p}^r)O^{''}(\mathbf{r}(t),\mathbf{p}^r(t))>_{\xi^{'}}}{<|Z|^{-1/2}>_{\xi^{'}}} \; , \end{aligned} \tag{35}$$

This general approach may now be directly applied to the calculation of the rate constant of a chemical reaction.

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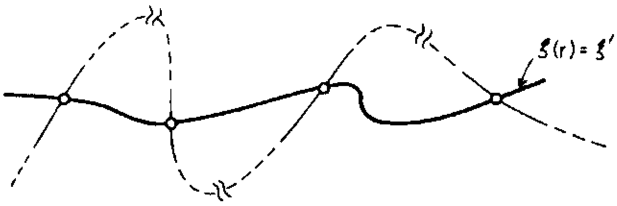

Figure 1: Schematic representation of Blue Moon sampling. The bold line represents the constrained ($\xi(\mathbf{r}) = \xi'$) dynamical evolution in phase space. The natural evolution of the system is indicated by the broken line. Open circles represent common points in configuration space which are the initial conditions of the activated trajectory sampling. Note that these points are not real crossings in phase space since the two trajectories differ in the momentum space. Interruptions of the broken line stand for long time segments in the natural trajectory and indicate that "crossings" are very rare events. The dynamics represented by the light lines in the vicinity of the crossing points gives the dynamical information needed in Eq. (35).

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