Sampling: intro to MD

and intro to enhanced sampling

How do we integrate Newton's Eqn's

① $\vec{q}(\tau+d\tau) \approx \vec{q}(\tau) + d\tau \frac{d\vec{q}}{dt}\Big|_{t=\tau} + \frac{d\tau^2}{2} \frac{d^2\vec{q}}{dt^2}\Big|_{t=\tau} + O(d\tau^3)$

$\approx \vec{q}(\tau) + d\tau\, \vec{v}(\tau) + d\tau^2/_2\, \vec{a}(t)$ [Remember: $d = vt + \frac{1}{2}at$

Remember $a_i(t) = -\frac{\partial U(q(t))}{\partial q_i} \cdot \frac{1}{m_i} \doteq F_i/m$

Also would need $v(\tau + d\tau)$, can do by finite diff

[$\vec{v} = d\vec{q}/d\tau \approx \frac{\vec{q}(t+d\tau) - \vec{q}(t)}{d\tau}$] or by expanding
$\vec{v}(t+d\tau) \approx \vec{v}(t) + d\tau\, \vec{a}(t) + O(d\tau^2)$, but people came up with schemes that are better.

Example, could have written:

no vel

② $\vec{q}(\tau - d\tau) = \vec{q}(\tau) - d\tau \frac{d\vec{q}}{dt}\Big|_{t=\tau} + \frac{d\tau^2}{2} \frac{d^2\vec{q}}{dt^2}\Big|_{t=\tau} + O(d\tau^3)$

add ①+② $\Rightarrow$ $\vec{q}(\tau+d\tau) + \vec{q}(\tau - d\tau) = 2\vec{q}(\tau) + d\tau^2/_m\, \vec{F}(t)$

③ $\frac{①-②}{d\tau} \Rightarrow \vec{v}(\tau) \approx (q(\tau + d\tau) - q(\tau - d\tau))/2d\tau$

Verlet 1967, alternate these two eqns

→ Good idea to have time reversibility
these equations are invariant under $d\tau \to -d\tau$

Another variant, using this backwards idea
$(q(\tau+d\tau), -v(\tau+d\tau)) \to \{q(\tau), -v(\tau)\}$

[note
$v = dq/dt$
$-v = dq/d(-t)$

④ $\vec{q}(\tau) = \vec{q}(\tau+d\tau) - d\tau\, \vec{v}(\tau+d\tau) + d\tau^2/_2\, \vec{F}(\tau)/_m$

⑤ Sub 1→4 $\Rightarrow$ $v(\tau+d\tau) = v(\tau) + \frac{d\tau}{2m}[F(\tau+d\tau) + F(\tau)]$

Alternate 1 & 5,

Lets go back to formal description

$$dP/dt = -\frac{\partial H}{\partial q} \qquad \frac{dq}{dt} = \frac{\partial H}{\partial p}$$

$$-i\mathcal{L}A = \{H, A\} = \sum_{i=1}^{N} \frac{\partial H}{\partial q_i}\frac{\partial}{\partial p_i} - \frac{\partial H}{\partial p_i}\frac{\partial}{\partial q_i}$$

$$dA/dt = \{A, H\}$$

$$\Rightarrow A(t) = e^{+i\mathcal{L}t} A(0),$$

can rewrite $\mathcal{L} = \mathcal{L}_p + \mathcal{L}_q$ ↙ analogous for N particles

$$+i\mathcal{L}_p = -\frac{\partial \mathcal{H}}{\partial q}\frac{\partial}{\partial p} \qquad +i\mathcal{L}_q = +\frac{\partial \mathcal{H}}{\partial p}\frac{\partial}{\partial q}$$

if $\mathcal{H} = p^2/2m + U$

$$\Rightarrow \cancel{+}i\mathcal{L}_p = +F\,\partial/\partial(mv) = +\frac{F}{m}\frac{\partial}{\partial v}$$

$$\Rightarrow +i\mathcal{L}_q = +v\,\partial/\partial q$$

Now, $e^{A+B} \neq e^A e^B$ unless $[A,B] = AB - BA = 0$
and can show that $[+i\mathcal{L}_p, +i\mathcal{L}_q] \neq 0$, don't commute

however
Trotter Factorization $e^{A+B} = \lim_{P \to \infty} \left[e^{A/2P} e^{B/P} e^{A/2P} \right]^P$

so $e^{+iLt} \approx \left[\underbrace{e^{+i\mathcal{L}_p \frac{\Delta t}{2}}}_{\underline{\underline{P}}} \underbrace{e^{+i\mathcal{L}_q \Delta t}}_{\underline{\underline{Q}}} \underbrace{e^{+iL_p \Delta t/2}}_{\underline{\underline{P}}} \right]^M + O(M \Delta t^3)$

$(\Delta t = t/M)$ $\qquad O(M\Delta t^3) = O(t \Delta t^2)$

(one scheme) $\qquad$ error increases w/ time

Now $e^{c\, d/dx} g(x) = g(x+c)$

why? $g(x+c) = g(x) + c \frac{d}{dx} g(x) + \frac{c^2}{2} \frac{d^2}{dx^2} g(x) + \cdots = e^{c\,d/dx} g(x)$

$e^{c\,d/dx} = 1 + c \frac{d}{dx} + \frac{c^2}{2} \frac{d^2}{dx^2} + \cdots$

Applying once to $A = \{q_0, v_0\}$, $\underline{\underline{P}} A = \{q_0, \overbrace{v_0 + F_0/m \, \Delta t/2}^{v_1}\}$ $\qquad F_0 = F(q_0)$

$\underline{\underline{Q}}\,\underline{\underline{P}} A = \{q_0 + v_1 \Delta t, v_0 + F_0/m \, \Delta t/2\} = \{\underbrace{q_0 + v_0 \Delta t + \frac{F_0}{m} \Delta t^2/2}_{q_1}, v_1\}$

$\underline{\underline{P}}\,\underline{\underline{Q}}\,\underline{\underline{P}} = \{q_0 + v_0 \Delta t + F_0 \Delta t^2/m, v_0 + \frac{F_0 + F_1}{2m} \Delta t\}$ $\quad$ velocity verlet again

Seems overly complicated, but this formulation allowed for many advanced methods to be derived using splitting schemes.

E.g. RESPA, evolve slow and fast forces separately, eg $U(q) = U_{spring}(q) + U_{other}(q)$ ← expensive

$$iL^{fast} = F^{fast}\frac{d}{dp} + iL_q \quad , \quad iL^{slow} = F^{slow}\frac{d}{dp}$$

Then can do $$e^{iLt} \approx \left[e^{iL^{slow} t/2n} \, e^{iL^{fast} t/n} \, e^{iL^{slow} t/2n} \right]^n$$ (Tuckerman 1992)

but $$\underbrace{e^{iL^{fast} t/n}}_{\delta t} \approx \left[e^{\frac{\delta t}{2n} F^{fast}\frac{d}{dp}} \, e^{\frac{\delta t}{n} v \frac{\partial}{\partial q}} \, e^{\frac{\delta t}{2n} F^{fast}\frac{d}{dp}} \right]^n$$

Can save a lot of computer time if long range forces vary slowly

Also, error in methods grow as $\Delta t^{2 \text{ or } 3}$, how small should Δt be. In practice, fin fastest motion in system, $\omega = \sqrt{k/m}$,

$\tau = 2\pi/\omega$, want $\Delta t < \tau$, maybe $\Delta t < \tau/5$

* C-H bond $\tau < 10\,fs$ so MD sims $\Delta t \sim 2\,fs$ w/ rigid CH ...

Enhanced Sampling

We said before that the time avg

$$\langle A \rangle = \lim_{N \to \infty} \frac{1}{N} \sum_{i=1}^{N} A(X_i) \quad \text{for } N \text{ mc samples}$$

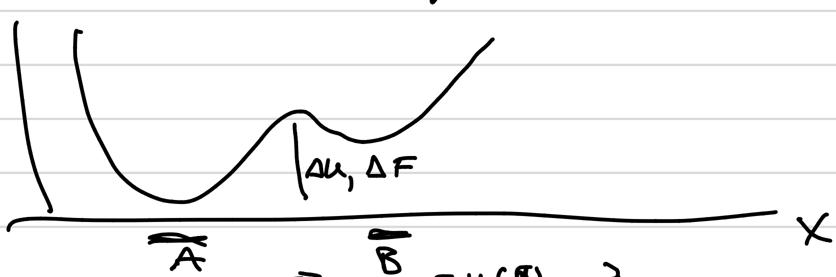
or $N = T/\Delta t$ md time steps is true if the system is ergodic, ie sees all the states

The problem in real simulation is $N \neq \infty$,

$N \sim (1 - 10^{10})$

This works for some problems, but there is a very common problem.

Suppose $U(x)$ or $F(x)$



$$F(\vec{x}) = -kT \log \int \delta(M(\vec{q}) - \vec{X})\, e^{-\beta u(\vec{q})} d\vec{q} - F_0$$

(Potential of mean force)

$$\text{Rate}_{A \to B} \propto e^{-\beta \Delta u^{\ddagger}} \text{ or } e^{-\beta \Delta F^{\ddagger}}$$