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A Format for Molecular Motor Analysis

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Real life confounded by vast array of temporal & spatial scales. Restricting to low resolution macro level is a) daunting
b) prone to introduce many effective parameters

Can one embed molecular motor analysis in traditional (but classical) many-body stat mech?

1

Truth in advertising:
What will not be done.

Will not focus on basic oscillating conformation cycle of motor.
Will not attend to models of transduction from this cycle to directed motion. Will aim at hopefully comfortable formulation of events leading up to above.

2

Perhaps suitable ensemble (multi realization) descriptions can smooth matters without completely losing control over microscopic basis.

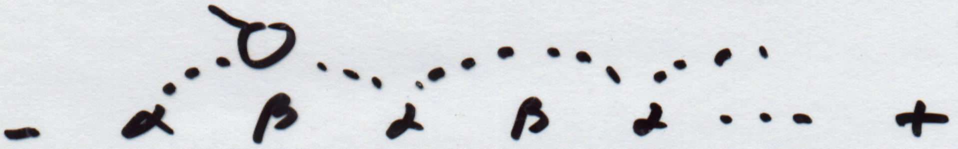
Will describe very incomplete study along these lines.

To deal with non-equilibrium, will make (first order in time scale) simplifications, with non-trivial consequences.

How much can we get away with, e.g. relying on ergodicity to transfer energy stochastically?

③

Useful to have in mind system illustrating phenomena without catchy image of molecules walking with two feet along filament. An



example is 1-head kinesin (based on motor domain C351 of KIF1 kinesin superfamily) with rapid processive motion on microtubule substrate. This is motivation, but won't get too close!

④

Blatantly general approach (don't mention Kachalski!). Start with closed system controlled by slow t-dependent $H(\epsilon t)$. Then

$$\dot{q} = [q, H(\tau)]$$

where $\tau = \epsilon t$

$$[A, B] \equiv \frac{\partial A}{\partial x} \cdot \frac{\partial B}{\partial p} - \frac{\partial A}{\partial p} \cdot \frac{\partial B}{\partial x}$$

$q = (x, p)$, $x = \{x_i\}$, $p = \{p_i\}$ implicit.

(Classical, but QM almost identical) and construct ensemble of realizations of dynamics, with probability density

$$\hat{\rho}(q, t)$$

5

By conservation of probability,

$$\frac{\partial \hat{\rho}}{\partial t} + \frac{\partial}{\partial q} \cdot \dot{q} \hat{\rho} = 0$$

so that

$$\frac{\partial}{\partial t} \hat{\rho}(q,t) + [q, H(\tau)] \cdot \frac{\partial}{\partial q} \hat{\rho}(q,t) = 0$$

$\epsilon \to 0$ regime singular, so need multi-time formulation $\hat{\rho}(q,t,\tau)$, highly underdetermined. Avoiding transients, only time scale τ should matter in this limit, so set

$$\hat{\rho}(q,t,\tau) = \rho_0(q,\tau) + \epsilon \rho_1(q,t,\tau) + \epsilon^2 \rho_2(q,t,\tau) + \cdots$$

and substitute:

$$\epsilon \frac{\partial \rho_0}{\partial \tau} + [\rho_0, H(\tau)] + \epsilon \frac{\partial \rho_1}{\partial t} + \epsilon [\rho_1, H(\tau)] \cdots = 0$$

(6)

Indeterminacy resolved by equating successive powers of ϵ:

a) $[\rho_0, H(\tau)] = 0$

b) $\frac{\partial \rho_0}{\partial \tau} + \frac{\partial \rho_1}{\partial t} + [\rho_1, H(\tau)] = 0, \cdots$

a) ρ_0 is constant of motion, so by assumed ergodicity,

$$\rho_0(\tau) = f(\tau, H(\tau))$$

b) Ability to solve for ρ_1 without diverging ρ_1 (absence of secular terms) determines f. First apply the operation

$$\mathrm{Tr}[\delta(E - H(\tau))(\quad)]$$

to b) for arbitrary E, where $\mathrm{Tr} \equiv \int d\mathrm{q}$:

⑦

$$\mathrm{Tr}\, \delta(E - H(\tau)) \frac{\partial}{\partial \tau} f(\tau, H(\tau))$$
$$+ \frac{\partial}{\partial t} \mathrm{Tr}\, \delta(E - H(\tau))\, \rho_1(t, \tau) = 0$$

Then apply the operation

$$\lim_{T \to \infty} \int_0^T \quad dT ,$$

assuming finiteness:

$$0 = \mathrm{Tr}\, \delta(E - H(\tau)) \frac{\partial}{\partial \tau} f(\tau, H(\tau))$$

or after a few steps,

$$\frac{\partial}{\partial \tau} f(\tau, E) \frac{\partial}{\partial E} W_\tau(E)$$
$$= \frac{\partial}{\partial E} f(\tau, E) \frac{\partial}{\partial \tau} W_\tau(E)$$

where

$$W_\tau(E) = \mathrm{Tr}\, \theta(E - H(\tau))$$
$$\equiv \exp S_\tau(E)$$

(8)

$S_\tau(E)$ is the entropy of the "broad-band" (microcanonical) partition function, and vanishing Jacobian above tells us that

$$f(\tau, E) = g(W_\tau(E))$$

for some function g. But suppose we know – to first order – the initial $\rho^{(0)}(H(0))$. Then, solving for g,

$$\rho_0(\tau) = \rho^{(0)}(W_0^{-1} W_\tau(H(\tau)))$$

explicit but not too transparent!

(9)

Dramatically simplified if

$\rho^{(0)}$ itself is broad-band microcanon:

$$\rho^{(0)}(H(0)) = \Theta(E_0 - H(0)) \,/\, W_0(E_0)$$

for we then verify at once that

$$\rho_0(\tau) = \Theta(E_\tau - H(\tau)) \,/\, W_\tau(E_\tau)$$

where the microcanonical E_τ is

defined by

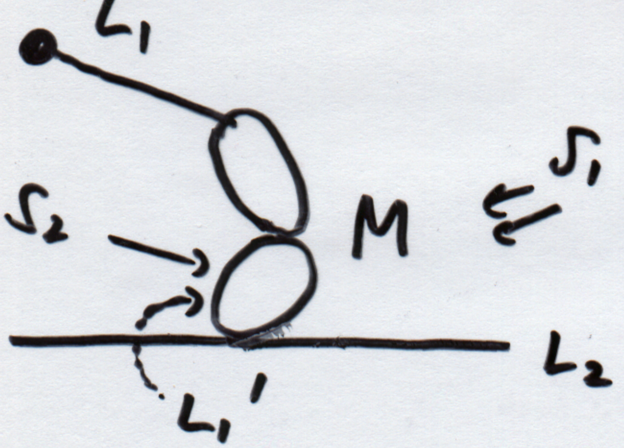
$$W_\tau(E_\tau) = W_0(E_0) :$$

$$S_\tau(E_\tau) = S_0(E_0).$$

Adiabatic at this level

implies isentropic

To this order, reversible, no heat liberated. Picked up at next order, involving equilibrium time correlations. Instead, we model dissipation and couple with other dissipations due to loads, to be balanced by energy sources, as in cartoon.



M = motor
loads L_1 & L_2
or
M' = M + L_2
loads L_1, L_2'

(11)

Dissipation expressed by non-conservative forces, due to neglecting lower level degrees of freedom. For this purpose, generalize Rayleigh dissipation function to

$$\dot{q} = J \frac{\partial H_0}{\partial q} - R_0 \frac{\partial H_0}{\partial q}$$

$J = \begin{pmatrix} 0 & I \\ -I & 0 \end{pmatrix}$, R_0 pos semi-def.

Then
$$\frac{dH_0}{dt} = \left(\frac{\partial H_0}{\partial q}\right)^T \left(J \frac{\partial H_0}{\partial q} - R_0 \frac{\partial H_0}{\partial q}\right)$$
$$= -\left(\frac{\partial H_0}{\partial q}\right)^T R_0 \frac{\partial H_0}{\partial q} \le 0.$$

Often constructed from non psd R_0; then use $H = H_0 + K$ with Kramers potential K to get form

$$\dot{q} = [q, H] - \gamma R \frac{\partial H}{\partial q}$$

with small parameter γ

With this dynamics, the Liouville equation becomes

$$\frac{\partial \rho}{\partial t} + [\rho, H] - \gamma \frac{\partial}{\partial q} \cdot \left(R \rho \frac{\partial H}{\partial q}\right) = 0$$

with time-independent H. We again set

$$\tau = \gamma t$$

$$\rho(t,\tau) = \rho_0(\tau) + \gamma \rho_1(t,\tau) + \ldots$$

and equate powers of γ:

a) $$0 = [\rho_0, H]$$

so

$$\rho_0(\tau) = f(\tau, H)$$

as previously.

13

b) $0 = \frac{\partial \rho_0}{\partial \tau} - \frac{\partial}{\partial q} \cdot \left(\rho_0 R \frac{\partial H}{\partial q} \right) + \frac{\partial \rho_1}{\partial t} + [\rho_1, H]$, ...

and again find $f(\tau, H)$

by applying

$$\lim_{T \to \infty} \frac{1}{T} \int_0^T \mathrm{Tr}\, \delta(E-H) \, (\quad) \, dt$$

Grinding the crank as before,

we now find

$$\frac{\partial f(\tau,E)}{\partial \tau} \frac{\partial W(E)}{\partial E} = \frac{\partial}{\partial E} \left(f(\tau,E) W_R(E) \right)$$

where

$$W(E) = \mathrm{Tr}\left(\theta(E-H) \right)$$

$$W_R(E) = \mathrm{Tr}\left(\theta(E-H) \frac{\partial}{\partial q} \cdot R \frac{\partial H}{\partial q} \right.$$

To solve, set

$$S_R(E) = \int^E dW(E)/W_R(E)$$

and now, for initial $\rho^{(0)}(E)$,

find the somewhat involved

$$\rho(\tau) = f(\tau, H)$$

$$= \frac{1}{W_R(H)} W_R S_R^{-1}(\tau + S_R(H)) \, \rho^{(0)}(S_R^{-1}(\tau + S_R(H))) .$$

However, if $\frac{\partial}{\partial q} \cdot R \frac{\partial H}{\partial q} = 1$, as in dissipative $F = -\gamma p$,

then $\rho(\tau) = e^{\tau} \rho^{(0)}(S^{-1}(\tau + S(H)))$,

minimizing entropy production,

since indeed one has

$$S(E) = -\mathrm{Tr}\, \rho^{(0)} \ln \rho^{(0)}$$

(15)

And if furthermore

$$\rho^{(0)}(H) = \theta(E_0 - H) / W(E_0)$$

then $\rho(\tau) = \theta(E_\tau - H) / W(E_\tau)$

with decaying energy E_τ defined by

$$S(E_\tau) = S(E_0) - \tau$$

$$\tau = \gamma t$$

Next we need energy sources - degrees of freedom $Q = (X, P)$, so

$$H(q,Q) = H(q) + H_I(q,Q) + \tilde{H}(Q)$$

and, confining energy dissipation to the motor system, we have on the full space

$$\rho(\tau) = \theta(E_\tau - H(q) - H_I(q,Q) - \tilde{H}(Q)) \cdot 1/W(E_\tau)$$

where $S(E_\tau) = S(E_0) - \tau$.

But of course we are interested in the projected q-space probability

$$\rho_q(\tau) = \mathrm{Tr}_Q\, \rho(\tau)$$

a) Special

$$H_I = 0,\ \tilde{H}(Q) = \Sigma\, P_i^2/2M$$

as in an ideal gas of sources in volume Ω. Just thermalization:

$$\mathrm{Tr}_Q\, \rho(\tau) = \Omega^N S_{3N} \cdot \int P^{3N-1}\theta(2M(E_\tau - H(q)) - P^2)\, dP$$

$$= C_N (1 - H(q)/E_\tau)^{3N}$$

$$\to C_N \exp -\left(\frac{3N}{E_\tau}\right) H(q)$$

But the decay of motor system energy is irrelevant as $N \to \infty$, and so

$$\rho_q(\tau) = \exp -\beta H(q) / \mathrm{Tr}_q \exp -\beta H(q),$$

corresponding e.g. to short time elastic H_2O collisions.

b) $$H_I(q,Q) = \sum_{i,j} \phi(x_i - X_j)$$

$$\tilde{H}(Q) = \sum_j \left(P_j^2/2M + h\{X_j^4 - X_j^2\}\right)$$

and then in the same fashion

$$\rho_q(\tau) = C \exp -\beta H(q)$$
$$\int \exp -\beta \sum_j \left(\sum_i \phi(x_i - X_j) + h(X_j)\right) \prod_j dX_j$$

Drop the internal h — no qualitative change — and so,

(18)

using the usual strategy for short range ϕ,

$$\int \exp - \beta \sum_i \phi(x_i - X_j)\ dX$$

$$= \int dX + \int [\exp - \beta \sum_i \phi(x_i - X) - 1]\ dX$$

$$= \Omega \left(1 + \frac{1}{\Omega} \int [\exp - \beta \sum_i \phi(x_i - X) - 1]\ dX\right)$$

from which we find at once

$$P_q(\tau) \to C' e^{-\beta H(q)}$$

$$\exp - \frac{N}{\Omega} \int [1 - \exp - \beta \sum_i \phi(x_i - X)]\ dX$$

This now couples any motor system states that are simultaneously in contact with a source, e.g. if Q_j must fit into a pocket.

19

Formally fine. But what is going on? If we could follow a realization in time, it would have a succession of dissipative propagations and excitations. This is precisely what the ensemble is doing, although invisibly for the non-descript thermalization.

But conformation-dependent interactions impart a local time-dependence to a realization. Projection onto a realization is the task now being tackled. - in the context of collective parameters of atomic aggregates.