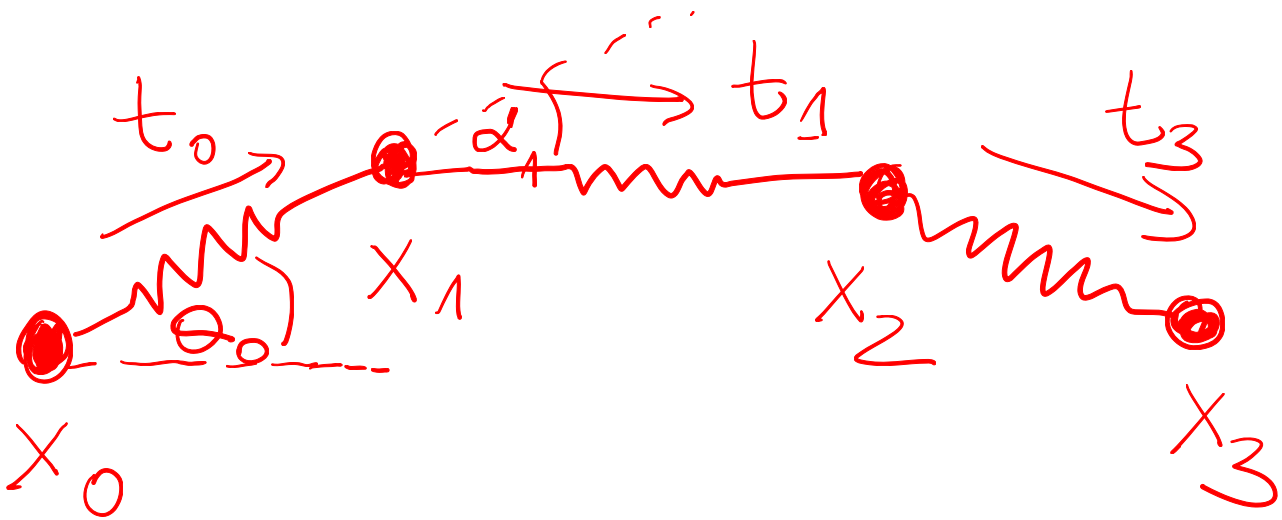
① Equilibrium Stat Mech of { Semiflexible Fibers / Worm-like chains

(e.g. polymers, DNA, actin, microtubules)



(2D)

$$\ell_j = \| x_{j+1} - x_j \| \qquad t_j = \frac{x_{j+1} - x_j}{\ell_j}$$

(2)

Energy due to <u>stretching</u>

$$E = \frac{k}{2} \sum_{j=0}^{N-1} \ell_j^2$$

spring constant

called "freely-jointed chain"

Statistical Mechanics dictates the equilibrium distribution (invariant measure) at thermodynamic equilibrium at temperature T be the Gibbs-Boltzmann Distribution

③

$$\underline{\bar{X}} = \{ x_i \} \text{ (configuration)}$$

$$P_{eq}(\underline{\bar{X}}) = Z^{-1} \exp\left(-\frac{E(\underline{\bar{X}})}{k_B T}\right)$$

Boltzmann's constant

But really GB is a Gibbs-Boltzmann weight and to make it into a distribution or measure we need a reference or base measure μ_0 :

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$$d\mu_{eq}(\underline{X}) = Z^{-1} \exp\left(-\frac{E(X)}{k_B T}\right) d\mu_0(\underline{X})$$

<u>Usually</u> $d\mu_0(\underline{X}) = d\underline{X}$ Lebesgue measure (volume)

Today we discuss an example (not unique!) where it is difficult if not impossible to define the base measure

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Part I

Bead-Link Chain

Often to a very good approximation the links of the chain are of fixed length

$$\|X_{j+1} - X_j\| = \ell_j = \ell \quad \left(\begin{array}{c}\text{inextensibility}\\ \text{constraint}\end{array}\right)$$

inextensible freely-jointed chain

What is $\lim_{k \to \infty} d\mu_{eq}(\bar{X})$???

(6) Now $d\mu_{eq}(\underline{X})$ is a measure on a <u>manifold</u>

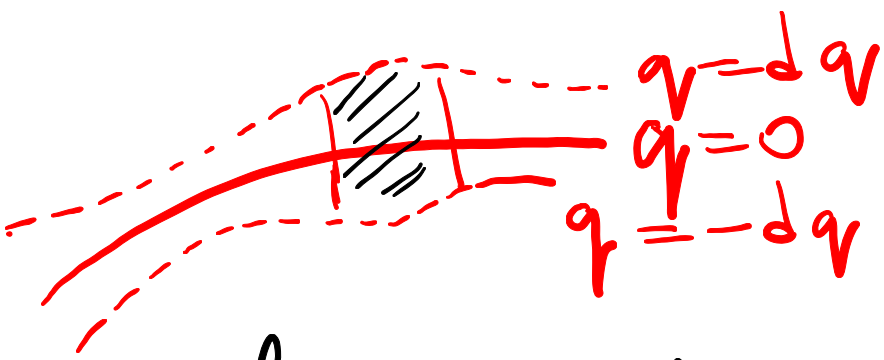
$$\mathcal{M} = \{ X \mid \ell_j = \ell, \forall j \}$$

If there is only stretching energy (freely-jointed chain) then $d\mu_{eq} = d\mu_0$

So what is the base measure?

⑦ Two options:

$$\begin{cases} ① \; d\mu_0(\underline{x}) = d\sigma_{\mathcal{M}}(\underline{x}) & \text{Hausdorff measure (area)} \\ ② \; d\mu_0(\underline{x}) = \prod_j \delta(\ell_j(\underline{x}) - \ell) \end{cases}$$



$$= \delta(q(\underline{x}))$$

where $\mathcal{M} = \{\underline{x} \mid q(\underline{x}) = 0\}$

$d\mu \sim$ area · "thickness" of manifold

⑧ The two are related by the <u>co-area formula</u>

$$\delta(q(x)) \cdot \|\nabla q(x)\| \, d\underline{\bar{x}} = d\sigma_{\mu}(\underline{\bar{x}})$$

Turns out the correct inextensible limit is

$$\begin{cases} d\mu_0 = \delta(q(\underline{\bar{x}}))\, d\underline{\bar{x}} \\ q_j = \ell_j^2 - \ell^2 \end{cases}$$

⑨ If there is an additional energy U (elastic, steric, electrostatic, etc.) then

$$d\mu_{eq}(\underline{X}) = e^{-U/k_BT}\, d\mu_0(\underline{X})$$

This has become complicated.

Why not just <u>avoid constraints</u>?

(10) If we know tangent vectors t_j then we know $\underline{X}$ if $X_0 = 0$

So why not use t's instead of X's ?

$$t_j = \{\cos\theta_j, \sin\theta_j\}$$

$$\theta_j \in [0, 2\pi)$$

and <u>θ's are unconstrained</u>

(11) At equilibrium, θ_j's are <u>uncorrelated</u> and <u>uniformly</u> distributed in $[0, 2\pi)$

$$d\mu_0(\vec{\theta}) = \prod_j \frac{d\theta_j}{2\pi}$$

this is simple and physically intuitive – we could have just started here (?)

Part 2

Worm-Like chain

(based in part on notes by Eric Vanden-Eijnden)

Let's now consider a chain that resists bending (most do, e.g., DNA)

Elastic bending energy:

$$U \equiv U_{bend} = \frac{2K}{\ell} \sum_{j=1}^{N-1} \sin^2\left(\frac{\alpha_j}{2}\right)$$

(semi-flexible fiber / worm-like chain)

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$$\cos \alpha_j = t_j \cdot t_{j-1}$$

$$\alpha_j = \theta_j - \theta_{j-1}$$

So we can use α's as configuration variables

$$(x_0, t_0, \vec{\alpha}) \longleftrightarrow \underline{\bar{X}}$$

Base measure is

$$d\mu_0(\vec{\alpha}) = \prod_j \frac{d\alpha_j}{2\pi}$$

(14)

$$d\mu_{eq}(\vec{\alpha}) = \prod_j \left(Z \exp\left(-\frac{2K}{\ell k_B T} \sin^2\left(\frac{\alpha_j}{2}\right)\right)\right) d\alpha_j$$

α's are <u>i.i.d</u> (product distribution)

If chain is "stiff" $\sin^2 \frac{\alpha_j}{2} \simeq \left(\frac{\alpha_j}{2}\right)^2$

and α's are Gaussian i.i.d

What does it mean for a chain to be stiff?

(Dimensionless parameter)

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$$\langle t_j \cdot t_{i+j} \rangle_{\mu_{eq}} = \left\langle \cos\left(\sum_{k=1}^{j} \alpha_k \right) \right\rangle_{\mu_{eq}}$$

can be done using $\alpha \ll 1$ approx.

$$\langle t_j \cdot t_{i+j} \rangle \approx e^{-(j\ell)/\xi} = e^{-s_j/\xi}$$

$s_j = j\ell$ = arc length (contour length)

$$\xi = \frac{2K}{k_B T}$$

persistence length (~50 nm for λ-DNA)

(16) Stiff chain means

$$\ell \ll \xi$$

In this case we can take a <u>continuum limit</u> $\frac{\ell}{\xi} \to 0$

$$\underline{X} \to \underline{X}(s) \in \mathbb{R}^3$$

$$s \in [0, L] = \text{arc length}$$

Recall $\alpha_j = \theta_j - \theta_{j-1}$

(17)

$$\frac{\alpha_i}{\ell} \longrightarrow \theta'(s_i)$$

$$t(s) = \underline{X}_s(s) = \{\cos(\theta(s)), \sin(\theta(s))\}$$

Is $\theta(s)$ is (almost surely) $\left\{\begin{matrix}\text{continuous} \\ \text{differentiable}\end{matrix}\right\}$ for $\forall s$?

For a stiff chain

$$\sin^2\left(\frac{\alpha_i}{2}\right) \simeq \left(\frac{\alpha_i}{2}\right)^2$$

(18)

$$U_{bend} \simeq \frac{K}{2\ell} \sum_{j=1}^{N-1} \alpha_j^2$$

$$\xrightarrow[\ell \to 0]{} \frac{K}{2} \int_{s=0}^{L} (\theta'(s))^2 \, ds$$

$$= \frac{K}{2} \int \|x''(s)\|^2 \, ds$$

$$U[x(\cdot)] = \frac{K}{2} \int_{s=0}^{L} \|x''(s)\|^2 \, ds \quad (2D/3D)$$

inverse curvature

Part 3

Continuum Brownian chains

What is the continuum limit of $\mu_{eq}(\underline{X})$ for a worm-like chain?

Physicists often (naively!) write

$$P_{eq}[\underline{X}(\cdot)] \sim \exp\left(-\frac{\mathcal{U}[\underline{X}(\cdot)]}{k_B T}\right) \mathcal{D}\underline{X}$$

"nonsense" notation (formal)

(20) But Lebesgue measure cannot be generalized to infinite dimensions (theorem), so $\mathcal{D}X$ is just formal notation with no clear meaning

<u>Functional distributions</u> don't usually make sense, <u>except</u> when they are Gaussian (we are in luck!)

(21) Let's work with $\theta(s)$ since $X(s)$ is constrained by $\|X_s\| = 1$ (inextensibility)

What does

$$P_{eq}[\theta(\cdot)] \sim \exp\left[-\frac{\xi}{4}\int_{s=0}^{L}(\theta'(s))^2\,ds\right]$$

persistence length

mean precisely?

(22) <u>Derivation #1</u>

discrete $\rightarrow$ continuum
(more physical for <u>modeling</u>)

Recall α_j's are i.i.d.
Gaussian random variables
with mean $\emptyset$ and variance $\frac{\xi}{4\ell}$:

$$d\mu_{eq}(\alpha_j) = Z^{-1} \exp\left(-\frac{\xi}{4\ell}\alpha_j^2\right) d\alpha_j$$

$$d\mu_{eq}(\vec{\alpha}) = \prod_j d\mu_{eq}(\alpha_j)$$

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$$\theta_{j+1} = \theta_j + \sqrt{\frac{2\ell}{\xi}}\, \mathcal{N}(0,1)$$

$$\theta(s+ds) = \theta(s) + \sqrt{\frac{2ds}{\xi}}\, \mathcal{N}(0,1)$$

$$d\theta(s) = \sqrt{\frac{2}{\xi}}\, d\mathcal{B}(s) \quad \text{(SDE)}$$

Brownian motion

$\theta(s) = \theta_0 + \mathcal{B}\left(\frac{2s}{\xi}\right)$ is (periodic) Brownian motion on $[0, 2\pi)$

(24) This works in 3D also:

The tangent vector $\vec{t}(s)$ performs Brownian motion on the unit circle (2D) / sphere (3D) with diffusion coefficient ξ^{-1}

This has a clear and precise mathematical meaning

(25) But observe that $\xi \to 0$ (freely-jointed chain) limit does <u>not</u> make sense ($X(s)$ (almost) nowhere differentiable)

therefore we <u>cannot</u> write

$$d\mu_{eq} = e^{-U/k_BT}\, \cancel{d\mu_0}$$

makes sense

does <u>not</u> make sense

(in continuum $\ell \ll \xi$)

Derivation #2

(continuum from the start, math not modeling)

For simplicity, take a ring polymer, $k_B T = 1$, $\xi = 2$, so $\theta(s \in [0, 2\pi))$ is periodic

Let $\mathcal{L}\theta \equiv -\theta''$

Hermitian SPD operator

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$$U[\theta(\cdot)] = \frac{1}{2}\int_0^{2\pi} (\theta'(s))^2 \, ds$$

$$= -\frac{1}{2}\int_0^{2\pi} \theta(s)\,\theta''(s)\, ds$$

$$= \frac{1}{2}\left(\theta, \mathcal{L}\theta\right)_{L_2:[0,2\pi)}$$

Go to Fourier space

$$\theta(s) \rightarrow \{\hat{\theta}_k\}$$

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$$U(\hat{\theta}) = \sum_{k=-\infty}^{\infty} \frac{k^2 \hat{\theta}_k^2}{2} \quad \text{(Parseval's theorem)}$$

$$\Downarrow$$

$$d\mu_{eq}(\hat{\theta}) = e^{-U(\hat{\theta})} d\hat{\theta}$$

$$= \prod_k e^{-\frac{k^2 \hat{\theta}_k^2}{2}} d\hat{\theta}_k$$

which makes sense even though infinite-dimensional <u>product distribution</u>

(29) $$\hat{\theta}_k \overset{d}{=} \mathcal{N}(0, k^{-2})$$

which is the spectrum of periodic Brownian motion!

So we get $\theta(s) \equiv$ (periodic) Brownian motion

<u>Note</u>: $\frac{d\mathcal{B}}{ds} \equiv \mathcal{W}$ (white noise)

$$\hat{\mathcal{W}}_k \overset{d}{=} \mathcal{N}(0,1) \Rightarrow \hat{\mathcal{B}}_k \overset{d}{=} \mathcal{N}(0, k^{-2})$$

(complex)

(30) The advantage of the "math" derivation is that it is obvious how to generalize to any <u>quadratic energy</u>

$$U[\theta] = \frac{1}{2}(\theta, \mathcal{L}\theta)$$

$$\theta(s) = \sum_j c_j \Psi_j(s)$$

random coefficients

eigenfunctions of $\mathcal{L}$

(31) $\mathcal{L}\psi_j = \lambda_j \psi_j \quad , \lambda_j > 0$

$$(\psi_i, \psi_j) = \delta_{ij}$$

$$\Rightarrow (\theta, \mathcal{L}\theta) = \sum_j \lambda_j c_j^2 \Rightarrow$$

$$d\mu_{eq}(\vec{c}) = \prod_j \exp\left(-\frac{\lambda_j c_j^2}{2k_B T}\right) dc_j$$

Gaussian functional distributions can be made sense of.

32 But we still don't know how to add <u>dynamics</u> (non-equilibrium stat mech)

Is there a continuum limit of Brownian dynamics, i.e. functional overdamped (multiplicative noise) Langevin eqs?