Microbead Rheology

Theory and Applications
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Single 1 μm Bead in Saltwater
Path Data

• Each path is a time series with x and y positions recorded at regular time intervals
  – The x-positions can be denoted: \(X(0 = t_0), X(t_1), X(t_2), \ldots, X(t_i), \ldots, X(T = t_N)\)

• \(t_N = T = \) total recording time of path data
  – Typically \(T = 30\) seconds for experiments in the Hill lab

• \(\tau = \) lag time (inter-observation time)
  – The first lag time is \(t_{i+1} - t_i = 1/\)frame rate (typically 60fps \(\rightarrow \tau = 1/60s\)), but we are often interested in multiples of this first lag time (2/60, 3/60, etc.)
  – Number of data points = \(N = T/\tau\)
Path Data

• We are interested in the properties of the increments, \( \Delta X_i = X(t_i + \tau) - X(t_i) \)
  
  – \( t_i \) for \( i = 0, 1, 2, \ldots, N - \tau \)
  
  – sometimes for multiples of \( \tau \), i.e. 2/frame rate, 3/frame rate, 4/frame rate, etc.

• For a given path and \( \tau = 1/\text{frame rate} \), we then have \( N - 1 \) increments in each coordinate

• What does the distribution of the \( x \)-increments look like for this salt water path...?
Van Hove Correlation Function, Single Salt Water Path

Number of Increments

Increments at $\tau = 1/60s$ ($\mu m$)
Van Hove Correlation Functions, Averaged Salt Water Pathway
Mean-Squared-Displacement (MSD)

• For a time series of positions, \( X(t_i) \) for \( i = 0, 1, 2, \ldots, N \), at a given lag time \( \tau \), the MSD is defined as:

\[
\langle \Delta r^2(\tau) \rangle = \frac{1}{N - \tau + 1} \sum_{i=0}^{N-\tau} \left[ X(t_i + \tau) - X(t_i) \right]^2
\]

• At each lag time, \( \tau \), the MSD is the variance of the corresponding van hove correlation function
MSD of 1\(\mu\)m Beads in Salt Water

\[ \text{MSD (\(\mu\)m}^2) \]

\[ \log_{10}(\text{MSD (\(\mu\)m}^2)) \]

\[ \log_{10}(\text{lag time, } \tau \ (\text{s})) \]

Experimental Mean MSD
Brownian Motion

• A simple continuous-time stochastic process
• In our applications, we are interested in the brownian motion as a *random walk* of a particle
  – Think of a drunken sailor who stumbles out of the bar with nowhere to go: he takes a sequence of steps, but randomly chooses an angle for each one. How far away from the bar is he after some amount of time? (on average)
Brownian Motion

- Regard each increment, $\Delta X_i = X(t_i + \tau) - X(t_i)$, as a random variable
  - $\Delta X_i \sim N(0, 2D\tau)$
  - The increments are independent (the particle doesn’t “remember” where it was)

$$MSD(\tau) = 2dD\tau, \ d = \text{dimensionality} \ (\text{Einstein, 1905})$$

$$D = \frac{k_B T}{6\pi \eta r}, \ k = \text{Boltzmann’s constant}, \ \eta = \text{viscosity}, \ r = \text{radius} \ (\text{Stokes-Einstein})$$

- Fluctuation-Dissipation: allows us to infer dissipation (macro) properties from observed fluctuations (micro) and vice versa
MSD of 1 μm Beads in Salt Water

- **Experimental Mean MSD**
- **Theoretical MSD**

**Axes:**
- MSD (μm²)
- lag time, τ (s)
Single 1 μm Beads in Saltwater and 3% HBE Mucus
Van Hove Correlation Functions, Averaged HBE 3% Paths

Increments at $\tau = \frac{1}{60}, \ldots, \frac{5}{60}$ s ($\mu$m)
Van Hove Correlation Functions, Averaged HBE 3% Paths

Number of Increments

Increments at $\tau = 1/60, \ldots, 5/60$ s ($\mu$m)
MSD of 1 μm Beads in Salt Water and 3% HBE Mucus

- Saltwater Mean MSD
- HBE Mean MSD

MSD (μm²)

lag time, τ (s)
MSD of 1\(\mu\)m Beads in Salt Water and 3% HBE Mucus
Fractional Brownian Motion

• A generalization of brownian motion
  – The distribution of increments is still Gaussian with mean 0, but they are no longer independent, i.e. they are correlated and have “memory”

• We introduce a parameter, $\alpha$, that captures the linear, but not necessarily $= 1$ scaling of the MSD:

$$MSD(\tau) = 2dD\tau^\alpha$$

• If $\alpha < 1$, this is called sub-diffusion
• If $\alpha > 1$, this is called super-diffusion
Properties of Variance

• For N random variables $X_i$ we have:

$$Var\left(\sum_{i=1}^{N} X_i\right) = \sum_{i=1}^{N} Var \left( X_i \right) + \sum_{i\neq j} Cov \left( X_i, X_j \right)$$

• In our setting, the N (+1) random variables are increments, $\Delta X_i$ in each coordinate, and their sum is our observed path

• Let's look at what happens to the variance of this sum in two cases...
Brownian Motion

\[ \Delta X_i = X(t_i + \tau) - X(t_i) = N(0, 2D\tau) \]

\[ \text{Var} \left( \sum_{i=1}^{N} \Delta X_i \right) = \sum_{i=1}^{N} \text{Var}(\Delta X_i) + \sum_{i \neq j} \text{Cov}(\Delta X_i, \Delta X_j) = \sum_{i=1}^{N} 2D\tau = 2ND\tau \]

\[ \text{Var} \left( X(t_N) - X(t_0) \right) = 2DT = 2ND\tau \]

• Since the variance of the sum of the smallest increments is equal to the variance of the largest increment, we see that the increments are independent, i.e. covariance = 0
Fractional Brownian Motion

\[ \Delta X_i = \sqrt{2D\tau^\alpha} N_i(0, V_{ij}) \], where \( V_{ij} \) is a covariance matrix (defined later).

\[
\text{Var} \left( \sum_{i=1}^{N} \Delta X_i \right) = \sum_{i=1}^{N} \text{Var}(\Delta X_i) + \sum_{i \neq j} V_{ij} = 2DT^\alpha N^{1-\alpha}
\]

\[
\text{Var} \left( X(t_N) - X(t_0) \right) = 2DT^\alpha
\]

• Here we see that the two variances are no longer equal and we see that the increments are now correlated, and covariance is non-zero.
Covariance for fBm

\[ \Delta X_i = \sqrt{2D\tau^\alpha} N_i(0, V_{ij}) \]

\[ V_{ij} = \frac{1}{2} \left[ |i - j + 1|^\alpha + |i - j - 1|^\alpha - 2|i - j|^\alpha \right] \]
Experimental Drift?

We should probably look at the particle paths, per movie...
3% HBE Particle Paths, Movie: 6
3% HBE Particle Paths, Movie: 19
Drift

- Due to fluid flow, microscope movement, other external forces, etc.
- For now, we assume it is linear (constant in time), and we update our fBm model:

\[ \Delta X_i = \mu \tau + \sqrt{2D\tau^\alpha} N_i(0, V_{ij}) \]

- So we see that paths are a “superposition” of a stochastic process, fBm, and a deterministic, linear drift, with velocity \( \mu \)
Fitting fBm to data using MLE

• Using our model of fBm + drift, we can simultaneously fit the parameters D, α, and μ to each experimental path using Maximum Likelihood Estimation

• This allows us to accurately recover the diffusive parameters, despite drift (if it is linear), and effectively characterize the viscoelastic fluid and re-construct a “true” MSD
Maximum Likelihood Estimation

- Suppose there are \( N \) i.i.d. observations, \( X_1, \ldots, X_N \) from an unknown probability density function with parameters, \( \theta \)
  
  - We want to find an estimate of \( \theta \)

- We define the *joint density* function for these observations as
  
  \[
  f(X_1, \ldots, X_N \mid \theta) = \prod_{i=1}^{N} f(X_i \mid \theta)
  \]

- Now, we regard the observations as parameters of this function, and \( \theta \) as a variable (free to vary), and we end up with the *likelihood*

  \[
  L(\theta; X_1, \ldots, X_N) = f(X_1, \ldots, X_N \mid \theta)
  \]
Maximum Likelihood Estimation

• In practice, we mostly use the \textit{log-likelihood}, which is the natural logarithm of the likelihood function

\[
\ln L(\theta; X_1,..., X_N) = \sum_{i=1}^{N} \ln f(X_i \mid \theta)
\]

• Using calculus (if we are lucky), we can take partial derivatives of the log-likelihood function and find \textit{maximum} values of the parameters we are interested in. Otherwise, we can use a minimization routine (fminsearch() in matlab) on the parameter of interest on the \textit{negative log-likelihood} function
Simulating fBm Paths

- Form the covariance matrix, \( \frac{1}{2}(|t|^\alpha + |s|^\alpha - |t - s|^\alpha) \)
- Compute the square root matrix, \( \Sigma \)
  (eigenvalue decomposition is what I use)
- Generate a vector, \( v \), of numbers drawn from a standard Gaussian distribution
- Let \( u = \sqrt{2D\Sigma v} \), this is our 1-dimensional fBm path
- Can easily add a linear drift by choosing a velocity, \( \mu \), multiplying by the corresponding time vector, and adding it element-wise to \( u \)
MSD of Simulated Paths in Water

- Theoretical MSD
- Simulated Mean MSD

MSD ($\mu$m$^2$) vs. lag time, $\tau$ (s)
Assignments

• 1) write code that simulates Brownian paths in 2-d (will have 3 inputs \((D, \tau, T)\) and should output a time series of positions in \(x\) and \(y\)

• 2) write code to calculate MSD (input is a 2-d path, output is a vector of lag times and a vector of corresponding mean-squared-displacements)

• 3) write code that finds the maximum likelihood estimate of \(D\) for a brownian path (input is a 2-d brownian path, and \(\tau\); output is an estimate of \(D\))