Diffusion dynamics from multi-point correlation functions
-
an mri perspective

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Magnetic Resonance
Prostate Cancer staging

1. Normal
2. Stage 1
3. Stage 2
4. Stage 3
5. Stage 4
Multi-phase and Multi-scale
98.9% fresh water from underground aquifers
Porous Media

• Intrinsically multi-phase materials, microstructure is important
  – Rocks, oil and water reservoirs
  – Soils, unconsolidated formation
  – Cement and concrete, catalysts
  – Foodstuff, paper, fabric
  – Plant and animal tissues, bone

• Pore fluids for NMR detection
MRI: Diffusion within pore space

Torrey-Bloch equation:

\[ \frac{\partial M}{\partial t} = D \cdot \nabla^2 M - \mu M \]

Boundary condition:

\[ D\vec{n} \cdot \nabla M = \rho M \]

Very large \( \rho \) \( \Leftrightarrow \) \( M=0 \) on the surface.

Eigenvalues and eigenfunctions are characteristics of the pore geometry.
Complex Diffusion Dynamics

• Natural samples
  – restricted diffusion + bulk diffusion + pore size distribution
  – Deviation of Gaussian diffusion
  – Fractals
MRI: Pulsed Field Gradient

\[ S(g) = \int f(x) \exp[-i q(x)] \, dx \]

- Displacement distribution
- 2-point correlation function

\[ q = \gamma gt \]

Stejskal & Tanner, JCP 1965, 1968
Restricted Diffusion
Fig. 1. Sample trajectories of

Figure 2 | Data for the six wandering albatross trips in 1992 that have known departure and return times. Red lines are hours for which a logger was completely dry; blue lines indicate hours when a logger was wet for some time.
FIG. 1 (color online). Time averaged mean squared displacement $\delta^2$ from individual trajectories of lipid granules in *S. pombe* in early mitotic (EM) cells (lower curves) and in early telophase (ET) (upper curves), measured by optical tweezers [34]. A distinct turnover from $\delta^2 \approx \Delta$ to $\approx \Delta^\beta$ ($\beta \approx 0.10 \ldots 0.20$) oc-
Multi-point Correlation
• How to distinguish restricted diffusion vs bulk diffusion?
  – $D(\Delta)$ vs $D(2\Delta)$

• How to identify non-Gaussian diffusion from diffusion distribution?
Multiple Encoding experiment

• High dimensionality of experiments
  – 6D for q1, q2
  – 3D for delays
Signal Equation

One molecule

\[ s(g_i) = \exp \left[ -i\gamma \sum_k g_k x_k \right] \]

Ensemble

\[ E(g_i) = \int f(x_k) \exp \left[ -i\gamma \sum_k g_k x_k \right] \]
Two-points

\[ s(g_i) = \left< \exp \left[ -i \gamma gt (x_1 - x_2) \right] \right> \]

\[ \sim \exp[-q^2 \frac{\langle x^2 \rangle_\Delta}{2}] \]

\[ = \exp[-q^2 D(\Delta)\Delta] \]

Diffusion time
Time-Dependent Diffusion

\[ D = \frac{\left\langle x(\Delta)^2 \right\rangle}{6\Delta} \]

**Diagram:**
- **Y-Axis:** Diffusion Coefficient
- **X-Axis:** Diffusion time
- **Graphs:**
  - Bulk
  - Open porous media
  - Drops

**Equation:**
\[ D = \frac{\left\langle x(\Delta)^2 \right\rangle}{6\Delta} \]

**Source:**
Sen, Concepts in Magnetic Resonance, 2004
Restricted diffusion

Short time

Long time

\[ \frac{D(t)}{D_0} \]

\[ \left( D_0 t \right)^{1/2} \text{ [\( \mu m \) ]} \]

Hurlimann
Multiple Encoding experiment

• Multiple correlations
  – D(Delta) and D(2Delta)
\[
\ln [E(q_1, q_2)] = -\Delta \left[ q_1^T \tilde{D}(\Delta) q_1 + q_2^T \tilde{D}(\Delta) q_2 + 2q_1^T (\tilde{D}(2\Delta) - \tilde{D}(\Delta)) q_2 \right]
\]
Signal Equation

\[ \ln [E(q_1, q_2)] = -\Delta [q_1^T \bar{D}(\Delta) q_1 + q_2^T \bar{D}(\Delta) q_2 + 2q_1^T (\bar{D}(2\Delta) - \bar{D}(\Delta)) q_2] \]

Jespersen and Buhl, JMR 2011
Paulsen et al., JMR 2014
Signal Equation

\[
\ln \left[ \frac{E(q_s, q_d)}{E(0, 0)} \right] = -\frac{\Delta}{2} \left[ q_s^T D_s q_s + q_d^T D_d q_d \right]
\]

\(q_s = q_1 + q_2\)
\(q_d = q_1 - q_2\)

\(D(2\Delta)\)
\(2D(\Delta) - D(2\Delta)\)
Eigenmodes: $q_s$ and $q_d$

$q_s = q_1 + q_2$
$q_d = q_1 - q_2$

$D(2\Delta) \approx D(\Delta)$
$q_s$ and $q_d$ decay

water

Avocado

Distilled Water

log ($s(q)$)

$q_d$

$q_s$

Avocado Sample

log ($s(q)$)

$q_d$

$q_s$ (cm$^{-1}$)

$|q|^2$ (cm$^{-2}$)
2D Diffusion Time Correlation

![Graphs showing 2D diffusion correlation](image_url)
Diffusion Time Correlation

- Off-Diagonal: Restricted Diffusion.
- Determine $D_0$ and $S/V$.

$$D_0 = \frac{\sqrt{2} \frac{D(\Delta) - D(2\Delta)}{\sqrt{2} - 1}}{\sqrt{2}}$$

$$\frac{S}{V} = \sqrt{\frac{(\sqrt{2} - 1)\pi}{\Delta}} \frac{D(\Delta) - D(2\Delta)}{\left(\sqrt{2} D(\Delta) - D(2\Delta)\right)^{3/2}}$$
Constant of Motion

Experimentally

\[ q_1 = q \cos(\phi) \hat{x}, \quad q_2 = q \sin(\phi) \hat{y}. \]

For isotropic D

\[ \ln [E (q, \phi)] \approx -\Delta q^2 D_\Delta. \]
Fourth order cummulant

\[
\exp\left[-i\phi\right] \sim \exp[-<\phi^2>-K<\phi^4>+...] 
\]

\[
\ln [E(q, \phi)] \approx -\frac{\Delta q^2}{2} ((D_{\Delta,xx} + D_{\Delta,yy}) + \cos(2\phi)(D_{\Delta,xx} - D_{\Delta,yy}) + 2\sin(2\phi)(D_{2\Delta,xy} - D_{\Delta,xy})) \\
- \frac{q^4}{4!} \left\{ 3 + \frac{\cos(4\phi)}{2} (K_{xxxx} + K_{yyyy}) + \frac{\cos(2\phi)}{2} (K_{xxxx} - K_{yyyy}) + \frac{3}{4} (1 - \cos(4\phi)) Z_{xxyy} \\
+ (\sin(2\phi) - \frac{1}{2} \sin(4\phi)) (S_{xxx} - S_{yy}) \right\} 
\]
Experimental results

Glass capillaries, 10 um diameter
Plant

0-th harmonics
Average diffusion

2-harmonics
Anisotropy

4-harmonics
Kurtosis
Diffusion Eigenmode Spectroscopy
MR Relaxation: T1 and T2
Diffusion Physics

Torrey-Bloch equation:

\[
\frac{\partial M}{\partial t} = D \cdot \nabla^2 M - \mu M
\]

Boundary condition:

\[
D \hat{n} \cdot \nabla M = \rho M
\]

Solution:

\[
M(x, t) = \sum_{n=0}^{\infty} A_n \phi_n(x) e^{-t/\tau_n}
\]

\[
A_n = \int dx \phi_n(x) M(x, 0)
\]

Eigenvalues and eigenfunctions are characteristics of the pore geometry.
Eigenfunctions & eigenvalues in an one-dimensional pore

$$\tau_0 \approx \frac{d}{\rho}$$

$$\tau_n = \frac{d^2}{\pi^2 Dn^2}$$

for

$$n = 1, 2, 3, ...$$
Diffusion modes

Isolated pores

Connected pores
Relaxation $\Leftrightarrow$ SVR

$$\frac{1}{T_1} = \frac{1}{T_{1b}} + \rho \frac{S}{V}$$

$$s(t) = s(0) \exp\left[-\frac{t}{T_1}\right]$$
Relaxation of Magnetization in a Rock

CPMG Decay for a Rock

Time, msec

Signal amplitude

Porosity

0.1 sec

0.00

0.40

0.1

1.0

10.0

100.0

1000.0

Signal Distribution

small pores

Pore Size

large pores

$T_2$, msec
New physics

Diffusion Eigenmodes to characterize pore structure
Relaxation $\rightarrow$ Decay

\[ s(t) = s(0) \exp\left[ -\frac{t}{T_1} \right] \]
Porous Beads vs Bulk Water

(B) Porous beads

τ₂ = 400 ms
320 ms
240 ms
80 ms
8 ms

(C) Bulk water

M(τ₁,τ₂)/M(0,τ₂)
Pack of Porous Grains

(A) pore size 0.3 µm
T1-T2 experiment

\[ \tau_1 \quad \tau_2 \]

T1-eigen modes  |  T2-eigen modes
T1-T2 experiment

\[ m_z(x) \] -1 \[ \sum_i a_i \phi_i^L \exp(-\tau_1 / T_{1i}) \] \[ \sum_i b_i \phi_i^T \exp(-\tau_2 / T_{2i}) \]
Signal $S(\tau_1, \tau_2)$

$$S(\tau_1, \tau_2) = \sum_{ij} <1|\phi_i^L><\phi_i^L|\phi_j^T> <\phi_j^T|1> \exp\left(-\frac{\tau_1}{T_{1i}} - \frac{\tau_2}{T_{2j}}\right)$$

This is the 2D Spectrum!

Diagonal signal -> $<\phi_i^L|\phi_i^T>$

Off-diagonal signal -> $<\phi_i^L|\phi_j^T>, i \neq j$
Physical Explanation

\[ \begin{align*}
\phi_{1,0} & \quad \phi_{1,1} \\
T_{2,0} \gg T_{2,1} & \\
\end{align*} \]
Physical Explanation

\[ m \propto e^{-\frac{T_{1,0}}{\tau_1}} \left| a_0 \phi_{1,0} \right| - e^{-\frac{T_{1,1}}{\tau_1}} \left| a_1 \phi_{1,1} \right| \]

Decay to zero
Diffusion Dynamics

Negative peak (1,0) distinguishes

Slow diffusion

Or

Pore size distribution

(1,0)

(0,0)

(1,1)

(0,1)

(0,2)
2D NMR ⇔ Eigenmode Spectroscopy

\[ S(\tau_1, \tau_2) = \sum_{ij} \langle 1 | \phi_i^L \rangle \langle \phi_i^L | \phi_j^T \rangle \langle \phi_j^T | 1 \rangle \exp\left(-\frac{\tau_1}{T_{1i}} - \frac{\tau_2}{T_{2j}}\right) \]

This is the 2D Spectrum!

Diagonal signal ->  \[ \langle \phi_i^L | \phi_i^T \rangle \]

Off-diagonal signal ->  \[ \langle \phi_i^L | \phi_j^T \rangle, i \neq j \]
Summary

• Higher order correlation functions can be measured and useful

• Experiments detect eigenmodes
Collaborators


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