From normal to anomalous deterministic diffusion
Part 3: Anomalous diffusion

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Sperlonga, 20-24 September 2010
yesterday:

2 From normal to anomalous deterministic diffusion:
   normal diffusion in particle billiards and anomalous diffusion in intermittent maps

note: work by T.Akimoto
yesterday:

- From normal to anomalous deterministic diffusion: normal diffusion in particle billiards and anomalous diffusion in intermittent maps

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today:

- Anomalous diffusion: generalized diffusion and Langevin equations, biological cell migration and fluctuation relations
Reminder: Intermittent map and CTRW theory

subdiffusion coefficient calculated from CTRW theory

**key:** solve Montroll-Weiss equation in Fourier-Laplace space,

\[
\hat{\varrho}(k, s) = \frac{1 - \tilde{w}(s)}{s} \frac{1}{1 - \hat{\lambda}(k)\tilde{w}(s)}
\]
Time-fractional equation for subdiffusion

For the lifted **PM map** $M(x) = x + ax^z \mod 1$, the MW equation in long-time and large-space asymptotic form reads

$$s^\gamma \hat{\varnothing} - s^{\gamma^{-1}} = -\frac{p\ell^2 a^\gamma}{2\Gamma(1-\gamma)\gamma^\gamma} k^2 \hat{\varnothing}, \quad \gamma := 1/(z-1)$$
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For the lifted PM map \( M(x) = x + ax^z \mod 1 \), the MW equation in long-time and large-space asymptotic form reads

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\hat{s} \gamma \hat{\rho} - \hat{s}^{\gamma-1} = -\frac{p \ell^2 a^\gamma}{2 \Gamma(1 - \gamma) \gamma} k^2 \hat{\rho}, \quad \gamma := 1/(z - 1)
\]

LHS is the Laplace transform of the Caputo fractional derivative

\[
\frac{\partial^\gamma \rho}{\partial t^\gamma} := \begin{cases} \frac{\partial \rho}{\partial t} & \gamma = 1 \\ \frac{1}{\Gamma(1-\gamma)} \int_0^t dt' (t - t')^{-\gamma} \frac{\partial \rho}{\partial t'} & 0 < \gamma < 1 \end{cases}
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\]

transforming the Montroll-Weiss eq. back to real space yields the time-fractional (sub)diffusion equation

\[
\frac{\partial^\gamma \rho(x, t)}{\partial t^\gamma} = K \frac{\Gamma(1+\alpha)}{2} \frac{\partial^2 \rho(x, t)}{\partial x^2}
\]
Interlude: What is a fractional derivative?

letter from Leibniz to L’Hôpital (1695): \( \frac{d^{1/2}}{dx^{1/2}} = ? \)

one way to proceed: we know that for integer \( m, n \)

\[
\frac{d^m}{dx^m} x^n = \frac{n!}{(n-m)!} x^{n-m} = \frac{\Gamma(n+1)}{\Gamma(n-m+1)} x^{n-m};
\]

assume that this also holds for \( m = 1/2, n = 1 \)

\[ \Rightarrow \frac{d^{1/2}}{dx^{1/2}} x = \frac{2}{\sqrt{\pi}} x^{1/2} \]
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fractional derivatives are defined via power law memory kernels, which yield power laws in Fourier (Laplace) space:

\[
\frac{d^\gamma}{dx^\gamma}F(x) \leftrightarrow (ik)^\gamma \tilde{F}(k)
\]

\(\exists\) well-developed mathematical theory of \textbf{fractional calculus};

see Sokolov, Klafter, Blumen, Phys. Today 2002 for a short intro
Deterministic vs. stochastic density

Initial value problem for fractional diffusion equation can be solved exactly; compare with simulation results for $P = \rho_n(x)$:

- Gaussian and non-Gaussian envelopes (blue) reflect intermittency
- Fine structure due to density on the unit interval $r = \rho_n(x) (n \gg 1)$ (see inset)
recall the escape rate theory of Lecture 1 expressing the (normal) diffusion coefficient in terms of chaos quantities:

$$D = \lim_{L \to \infty} \left( \frac{L}{\pi} \right)^2 \left[ \lambda(\mathcal{R}_L) - h_{KS}(\mathcal{R}_L) \right]$$

**Q:** Can this also be worked out for the subdiffusive PM map?
recall the escape rate theory of Lecture 1 expressing the (normal) diffusion coefficient in terms of chaos quantities:

\[ D = \lim_{L \to \infty} \left( \frac{L}{\pi} \right)^2 \left[ \lambda(R_L) - h_{KS}(R_L) \right] \]

**Q:** Can this also be worked out for the subdiffusive PM map?

1. solve the previous fractional subdiffusion equation for absorbing boundaries: can be done
2. solve the Frobenius-Perron equation of the subdiffusive PM map: ?? (∃ methods by Tasaki, Gaspard (2004))
3. even if step 2 possible and modes can be matched: ∃ an anomalous escape rate formula ???

two big open questions...
Motivation: biological cell migration

Brownian motion

3 colloidal particles of radius 0.53 μm; positions every 30 seconds, joined by straight lines (Perrin, 1913)
Motivation: biological cell migration

Brownian motion

3 colloidal particles of radius $0.53\mu m$; positions every 30 seconds, joined by straight lines (Perrin, 1913)

single biological cell crawling on a substrate (Dieterich, R.K. et al., PNAS, 2008)

Brownian motion?
Our cell types and how they migrate

MDCK-F (Madin-Darby canine kidney) cells

two types: wildtype ($NHE^+$) and NHE-deficient ($NHE^-$)

movie: NHE+: $t=210$ min, $dt=3$ min
Our cell types and how they migrate

MDCK-F (Madin-Darby canine kidney) cells

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movie: \(NHE^+: t=210\text{min, } dt=3\text{min}\)

note: the \textit{microscopic origin} of cell migration is a \textbf{highly complex process} involving a huge number of proteins and signaling mechanisms in the \textit{cytoskeleton}, which is a complicated \textit{biopolymer gel} – we do not consider this here!
Sequences of microscopic phase contrast images are segmented to obtain the cell boundaries.

1. Image processing
   (~ 100-1000 MB)
3. Cell outlines (own JAVA programs)
4. Cell trajectory
4’. Perimeter, area, structure index
Theoretical modeling: the Langevin equation

**Newton’s law** for a particle of mass $m$ and velocity $v$ immersed in a fluid

$$m\ddot{v} = F_d(t) + F_r(t)$$

with total force of surrounding particles decomposed into *viscous damping* $F_d(t)$ and *random kicks* $F_r(t)$
Theoretical modeling: the Langevin equation

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Suppose $F_d(t)/m = -\kappa \dot{v}$ and $F_r(t)/m = \sqrt{\zeta} \xi(t)$ as Gaussian white noise of strength $\sqrt{\zeta}$:

$$\dot{v} + \kappa v = \sqrt{\zeta} \xi(t)$$

Langevin equation (1908)

‘Newton’s law of stochastic physics’: apply to cell migration?

**Note:** Brownian particles *passively* driven, whereas cells move *actively* by themselves!
Solving Langevin dynamics

calculate two important quantities (in one dimension):

1. the diffusion coefficient $D := \lim_{t \to \infty} \frac{msd(t)}{2t}$

with $msd(t) := \langle [x(t) - x(0)]^2 \rangle$; for Langevin eq. one obtains $msd(t) = 2 v_{th}^2 \left(t - \kappa^{-1}(1 - \exp(-\kappa t))\right)/\kappa$ with $v_{th}^2 = kT/m$

note that $msd(t) \sim t^2 \ (t \to 0)$ and $msd(t) \sim t \ (t \to \infty) \Rightarrow \exists D$
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2. the **probability distribution function** \(P(x, v, t):\)

- Langevin dynamics obeys (for \(\kappa \gg 1\)) the **diffusion equation**

\[
\frac{\partial P}{\partial t} = D \frac{\partial^2 P}{\partial x^2}
\]

solution for initial condition \(P(x, 0) = \delta(x)\) yields **position distribution** \(P(x, t) = \exp(-\frac{x^2}{4Dt}) / \sqrt{4\pi Dt}\)
Fokker-Planck equations

- for velocity distribution $P(v, t)$ of Langevin dynamics one can derive the Fokker-Planck equation

$$\frac{\partial P}{\partial t} = \kappa \left[ \frac{\partial}{\partial v} v + v_{th}^2 \frac{\partial^2}{\partial v^2} \right] P$$

stationary solution is $P(v) = \exp\left(-\frac{v^2}{2v_{th}^2}\right)/\sqrt{2\pi v_{th}}$
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- Fokker-Planck equation for position and velocity distribution $P(x, v, t)$ of Langevin dynamics is the Klein-Kramers equation

$$\frac{\partial P}{\partial t} = -\frac{\partial}{\partial x} [vP] + \kappa \left[ \frac{\partial}{\partial v} v + v_{th}^2 \frac{\partial^2}{\partial v^2} \right] P$$

the above two eqns. can be derived from it as special cases.
Experimental results I: mean square displacement

- $msd(t) := < [x(t) - x(0)]^2 > \sim t^\beta$ with $\beta \to 2$ ($t \to 0$) and $\beta \to 1$ ($t \to \infty$) for Brownian motion; $\beta(t) = d \ln msd(t)/d \ln t$

- **solid lines**: (Bayes) fits from our model

\[ \begin{array}{c|c|c|c|c}
\text{msd}(t) & \text{data:NHE}^+ & \text{data:NHE}^- & \text{FKK model:NHE}^+ & \text{FKK model:NHE}^- \\
\hline
\text{I} & \text{data:NHE}^+ & \text{data:NHE}^- & \text{FKK model:NHE}^+ & \text{FKK model:NHE}^- \\
\text{II} & \text{data:NHE}^+ & \text{data:NHE}^- & \text{FKK model:NHE}^+ & \text{FKK model:NHE}^- \\
\text{III} & \text{data:NHE}^+ & \text{data:NHE}^- & \text{FKK model:NHE}^+ & \text{FKK model:NHE}^- \\
\end{array} \]

anomalous diffusion if $\beta \neq 1$ ($t \to \infty$): here superdiffusion
Experimental results II: position distribution function

- $P(x, t) \rightarrow \text{Gaussian } (t \rightarrow \infty)$ and kurtosis
- $\kappa(t) := \frac{\langle x^4(t) \rangle}{\langle x^2(t) \rangle^2} \rightarrow 3 \ (t \rightarrow \infty)$ for Brownian motion (green lines, in 1d)
- other solid lines: fits from our model; parameter values as before

⇒ crossover from peaked to broad non-Gaussian distributions
The generalized model

- Fractional Klein-Kramers equation (Barkai, Silbey, 2000):

\[
\frac{\partial P}{\partial t} = -\frac{\partial}{\partial x} [vP] + \frac{\partial^{1-\alpha}}{\partial t^{1-\alpha}} \kappa \left[ \frac{\partial}{\partial v} v + v_{th}^2 \frac{\partial^2}{\partial v^2} \right] P
\]

with probability distribution \( P = P(x, v, t) \), damping term \( \kappa \), thermal velocity \( v_{th}^2 = kT / m \) and Riemann-Liouville fractional derivative of order \( 1 - \alpha \)

for \( \alpha = 1 \) Langevin’s theory of Brownian motion recovered
The generalized model

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with probability distribution \( P = P(x, v, t) \), damping term \( \kappa \), thermal velocity \( v_{th}^2 = kT/m \) and Riemann-Liouville fractional derivative of order \( 1 - \alpha \) for \( \alpha = 1 \) Langevin’s theory of Brownian motion recovered

- **analytical solutions** for \( msd(t) \) and \( P(x, t) \) can be obtained in terms of special functions (Barkai, Silbey, 2000; Schneider, Wyss, 1989)

- **4 fit parameters** \( v_{th}, \alpha, \kappa \) (plus another one for short-time dynamics)
Possible physical interpretation

- physical meaning of the fractional derivative?

A fractional Klein-Kramers equation can *approximately* be related to a generalized Langevin equation of the type

\[
\dot{v} + \int_0^t dt' \kappa(t - t') v(t') = \sqrt{\zeta} \xi(t)
\]

e.g., Mori, Kubo, 1965/66

with time-dependent friction coefficient \( \kappa(t) \sim t^{-\alpha} \)

cell anomalies might originate from soft glassy behavior of the cytoskeleton gel, where power law exponents are conjectured to be universal (Fabry et al., 2003; Kroy et al., 2008)
Possible biological interpretation

- biological meaning of anomalous cell migration?

Experimental data and theoretical modeling suggest *slower diffusion for small times* while *long-time motion is faster*

Compare with *intermittent optimal search strategies* of foraging animals (Bénichou et al., 2006)

*Note:* There is current controversy about *Lévy hypothesis* for optimal foraging of organisms (albatross, fruitflies, bumblebees,...)
Fluctuation relations

system evolving from an initial state into a nonequilibrium state; measure pdf $\rho(W_t)$ of entropy production $W_t$ during time $t$:

$$\ln \frac{\rho(W_t)}{\rho(-W_t)} = W_t$$

 transient fluctuation relation (TFR)

Evans, Cohen, Morriss (1993); Gallavotti, Cohen (1995)

1. generalizes the Second Law to small noneq. systems
2. yields nonlinear response relations
3. connection with fluctuation dissipation relations (FDR)
Fluctuation relations

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$$\ln \frac{\rho(W_t)}{\rho(-W_t)} = W_t$$  \textbf{transient fluctuation relation (TFR)}

Evans, Cohen, Morriss (1993); Gallavotti, Cohen (1995)

1. generalizes the \textbf{Second Law} to small noneq. systems
2. yields \textbf{nonlinear response relations}
3. connection with \textbf{fluctuation dissipation relations (FDR)}

\textbf{example:} check the above TFR for Langevin dynamics with constant field $F$; $W_t = Fx(t)$, $\rho(W_t) \sim \rho(x, t)$ is Gaussian

TFR holds if $<W_t> = <\sigma^2_{W_t} > / 2$ (FDR1)

for Gaussian stochastic process: $\text{FDR2} \Rightarrow \text{FDR1} \Rightarrow \text{TFR}$
An anomalous fluctuation relation

check TFR for the **overdamped generalized Langevin equation**

\[
\dot{x} = F + \xi(t)
\]

with \( < \xi(t)\xi(t') > \sim |t - t'|^{-\beta} \), \( 0 < \beta < 1 \): no FDT2

\( \rho(W_t) \) is Gaussian with \( < W_t > \sim t \), \( < \sigma^2_{W_t} > \sim t^{2-\beta} \): no FDT1 and superdiffusion

\[
\ln \frac{\rho(W_t)}{\rho(-W_t)} = C_{\beta} t^{\beta-1} W_t
\]

\( 0 < \beta < 1 \)

**anomalous TFR**

An anomalous fluctuation relation

check TFR for the **overdamped generalized Langevin equation**

\[ \dot{x} = F + \xi(t) \]

with \( < \xi(t)\xi(t') > \sim |t - t'|^{-\beta} \), \( 0 < \beta < 1 \): **no FDT2**

\( \rho(W_t) \) is Gaussian with \( < W_t > \sim t \), \( < \sigma^2_{W_t} > \sim t^{2-\beta} \): **no FDT1** and superdiffusion

\[
\ln \frac{\rho(W_t)}{\rho(-W_t)} = C_\beta t^{\beta - 1} W_t
\]

\( 0 < \beta < 1 \)

**anomalous TFR**


*note:* we see this aTFR in experiments on cell migration

Hayashi, Takagi (2007)

experiments on slime mold:


Hayashi, Takagi (2007)

**note:** we see this aTFR in experiments on cell migration

Dieterich, Chechkin, Schwab, R.K., tbp
Summary

- **Microscopic**
  - Dynamical systems
  - Statistical mechanics

- **Macroscopic**
  - Thermodynamics

- **General theory of nonequilibrium statistical physics**
  - Deterministic transport
  - Thermodynamic properties
  - Fractal SRB measures
  - Infinite measures

- **Microscopic chaos**
  - Ergodic hypothesis
    - Strong
    - Weak

- **Complexity**
  - Normal
  - Anomalous

- **Nonequilibrium conditions**
  - Equilibrium
  - Nonequilibrium steady states
  - Nonequilibrium non-steady states

- Weakly chaotic map
- Anomalous cell migration
- Fluctuation relations
- Conclusions

From normal to anomalous diffusion 3
work performed with:
C.Dellago, A.V.Chechkin, P.Dieterich, P.Gaspard, T.Harayama, P.Howard, G.Knight, N.Korabel, A.Schüring

background information to:
Part 1,2

and for cell migration: Dieterich et al., PNAS 105, 459 (2008)