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The statistics of particle tracking: a linchpin in countless biophysics experiments

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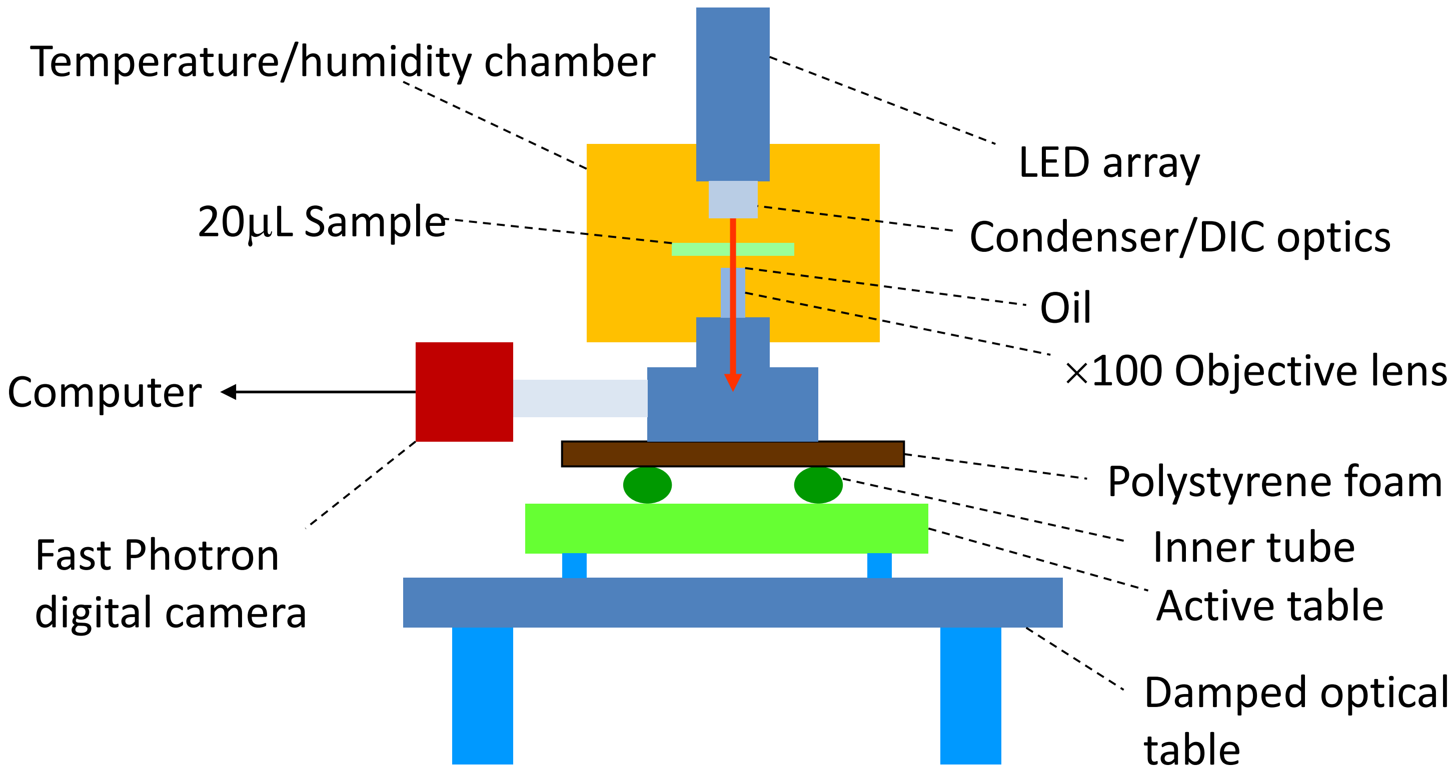
A tracking experiment

Optical microscopy

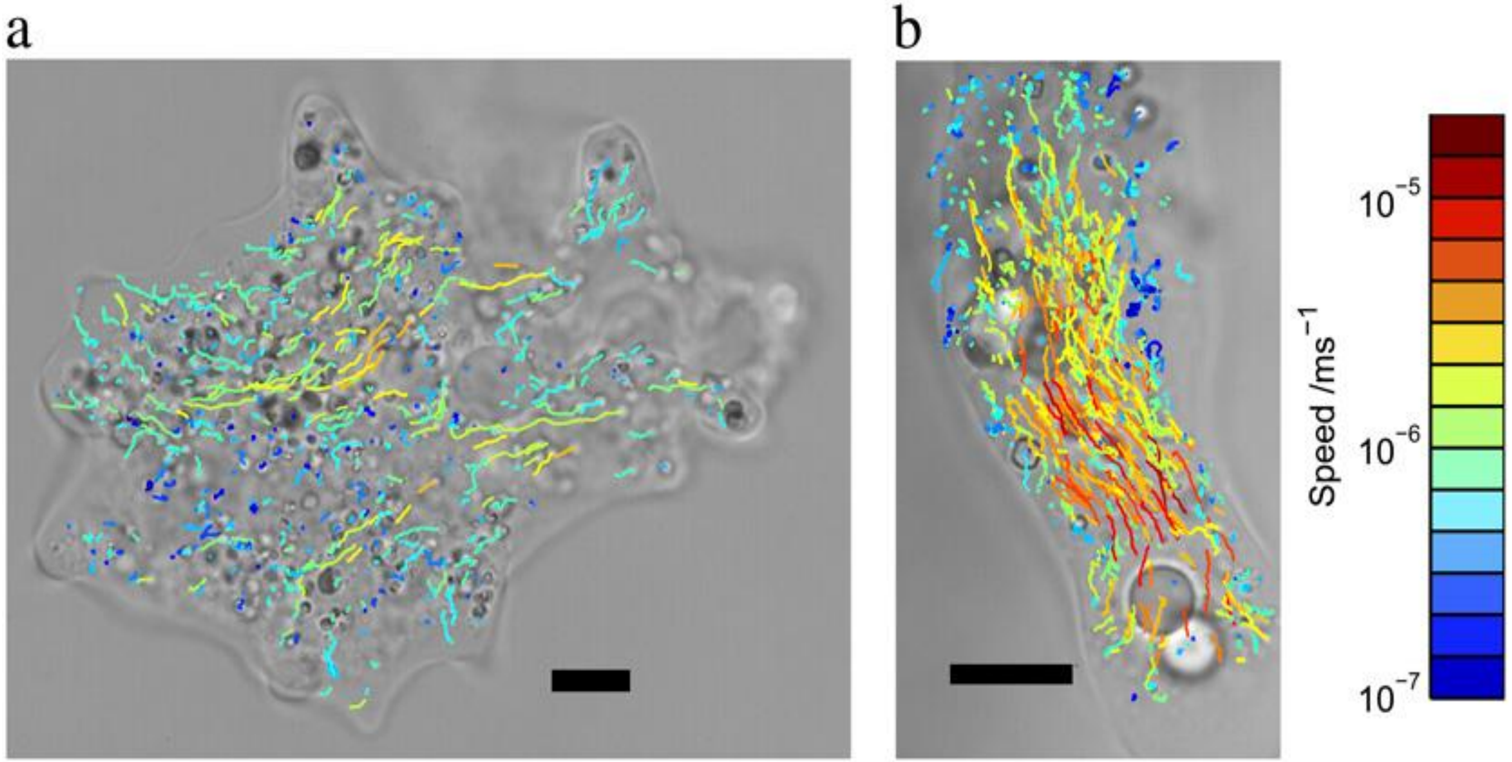


Also: CERN, X-ray imaging, astrophysics (satellites) etc.

A linked list of displacements = a track

Samples

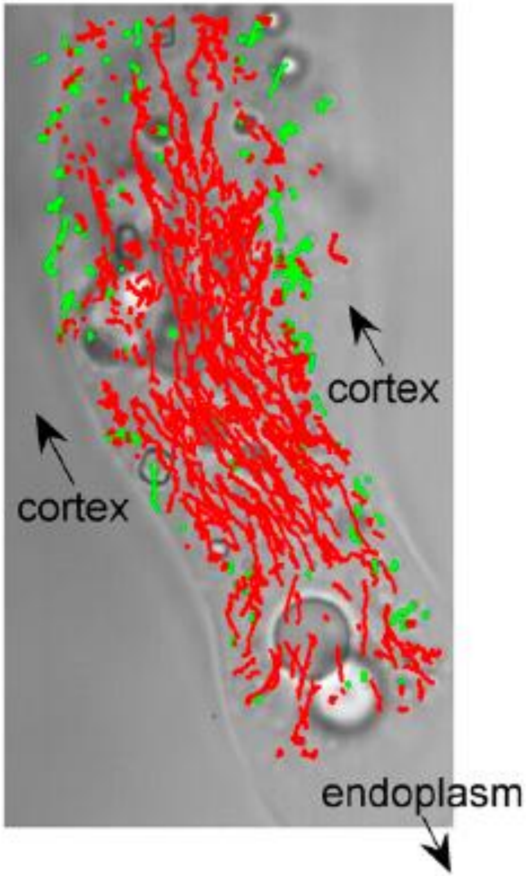
Synthetic soft matter, biomolecules, motor proteins, single molecules, live cells

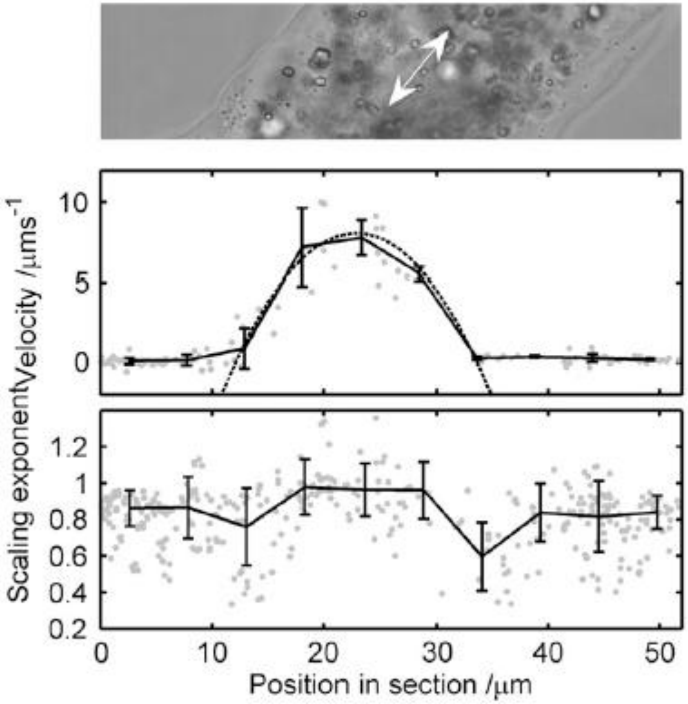


Thousands of organelles moving around at 0.00001s!

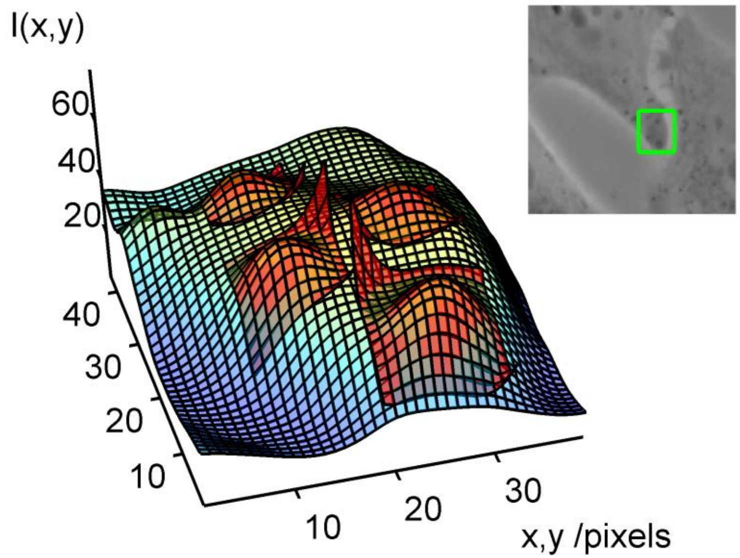
S.Rogers, T.A.Waigh, J.Lu, *Biophysical Journal*, 2008, 94, 3313-3322.

Cytoplasmic streaming





Software – polyparticletracker

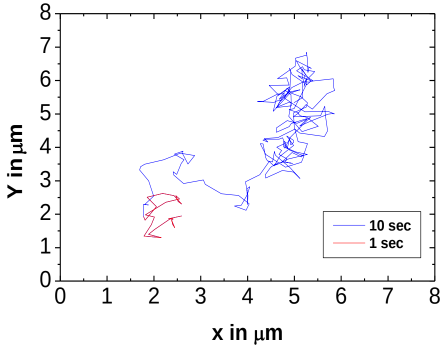


Advantages:

Good for cells,
Works well with fluorescence at low copy numbers,
Can be used with huge data sets from fast cameras (100,000 fps),
Parallel versions now exist,
It is freely available.

S.S.Rogers, et al, *Physical Biology*, 2007, 4, 220-227.

Analysis: What do we do with the tracks?



For Brownian motion

$$\langle \Delta r(t) \rangle = 0$$

Mean square displacement

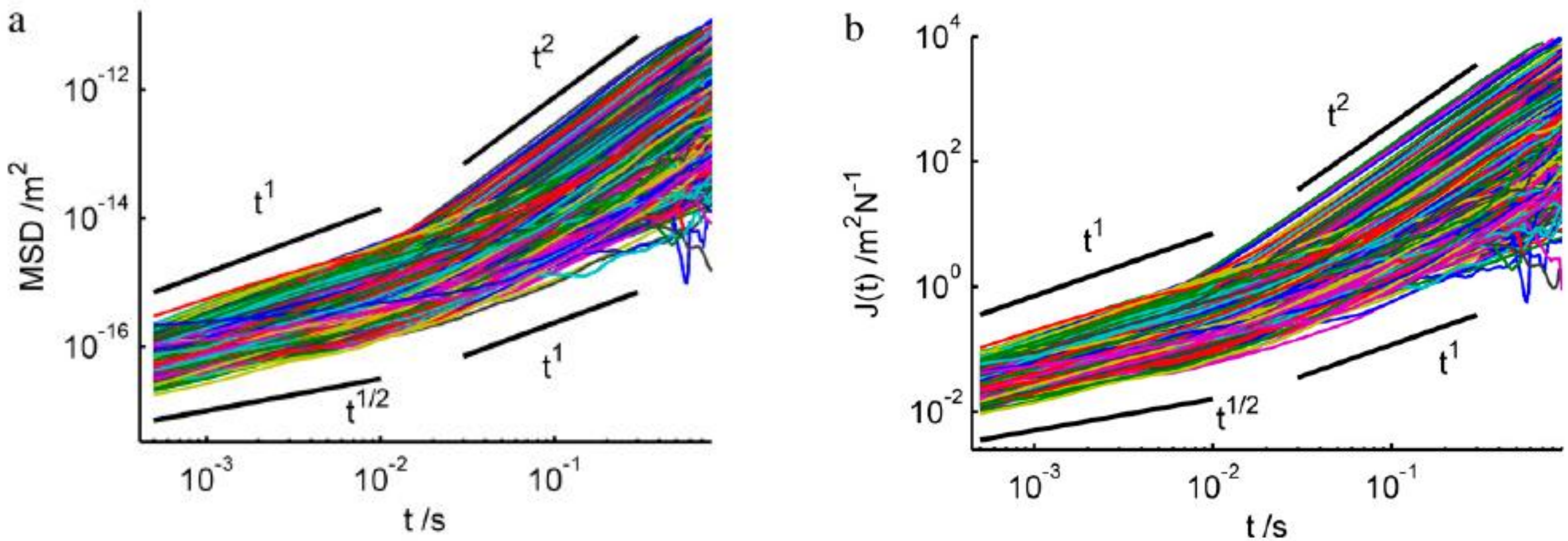
$$\langle \Delta r^2(t) \rangle = 4Dt$$

Einstein 1905

Perrin 1926 – Nobel Prize

Beware of defining a velocity v=r/t for stochastic processes!

The many uses of MSDs



Useful measure of stochastic motion.

Linearly proportional to the compliance ($J(t) = \frac{\pi a}{kT}\langle \Delta r^2(t)\rangle = \frac{e(t)}{\sigma(t)}$). Leads to microrheology. Huge range of uses e.g. examine mucus in the intestines, antibiotic resistant bacteria, heart muscle etc.

What else is possible?

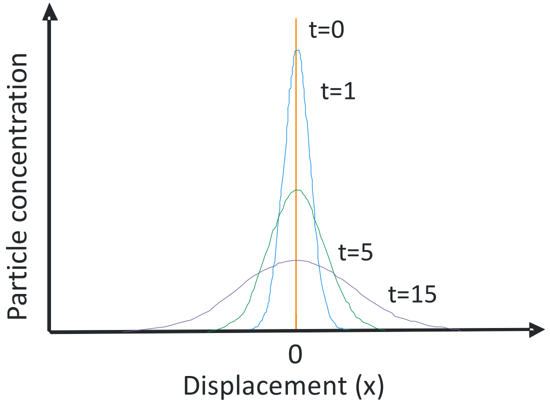
Calculate higher moments,

$\langle r^3 \rangle$, how skew the distribution is.

$\langle r^4 \rangle$, kurtosis, how non-Gaussian the distribution is.

……. Moment generating function.

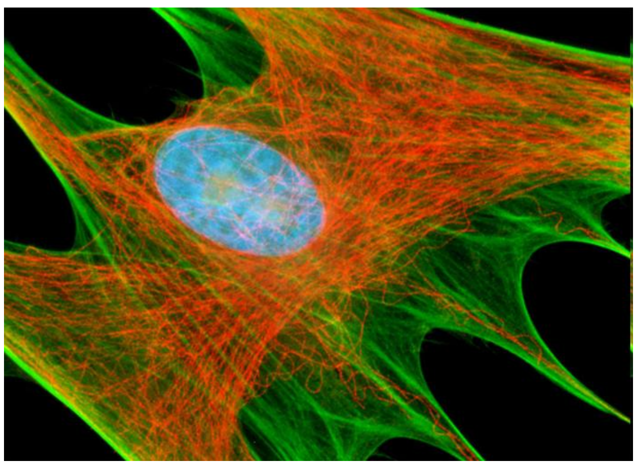
Full probability distribution function.

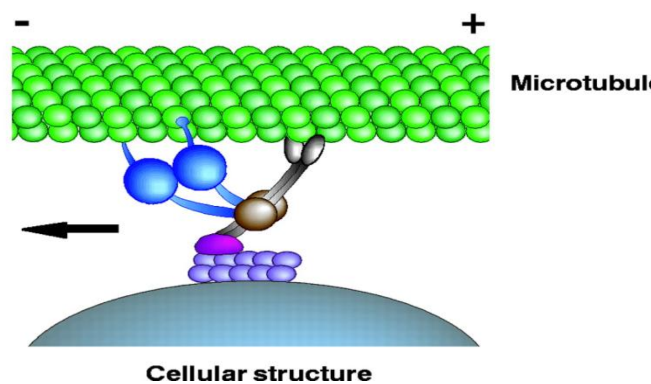


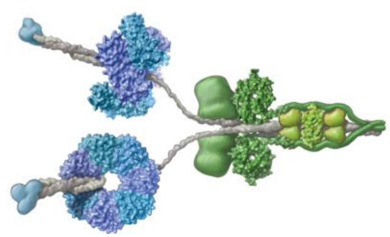
Or its Fourier Transform, intermediate scattering function.

2 crucial unanswered questions in cellular biology : vesicle transport dynamics

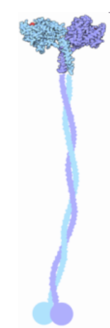
1) Tug of war model.
2) Nature of subdiffusive motion at short times in cells: many models - *ant in a fractal labyrinth*, *fractional Brownian motion*, *continuous time random walk*.







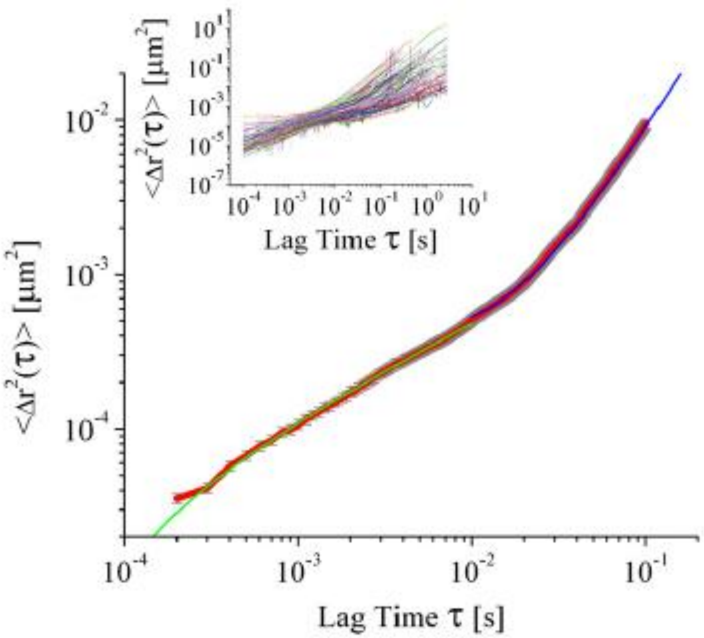
Dynein

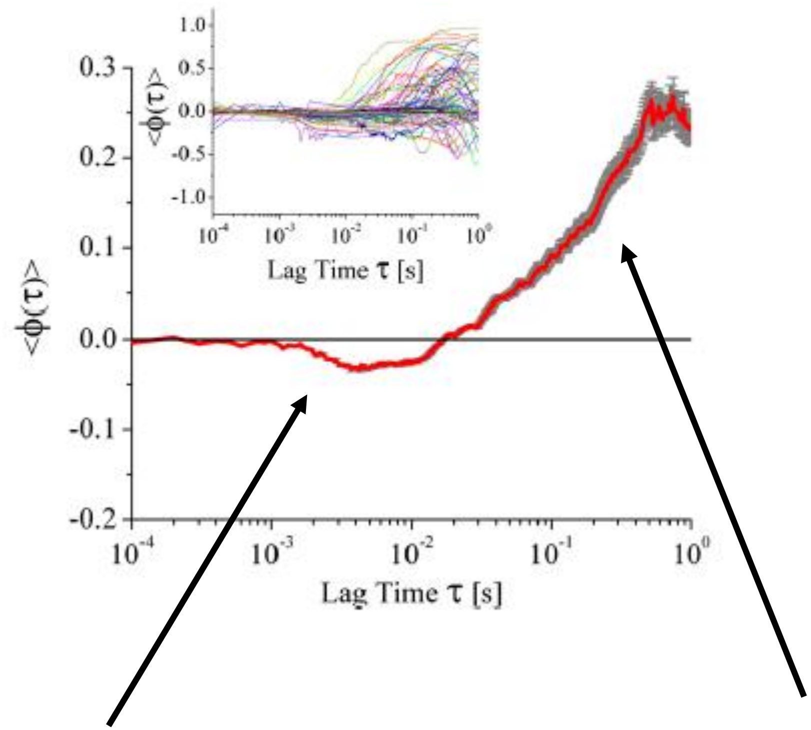


Kinesin

Angular corrections

$$\langle\phi(\tau)\rangle = \langle\cos\theta(\tau)\rangle = \frac{\underline{r_1}(\tau).\underline{r_2}(\tau)}{\left|\underline{r_1}(\tau)\right|\left|\underline{r_2}(\tau)\right|}$$





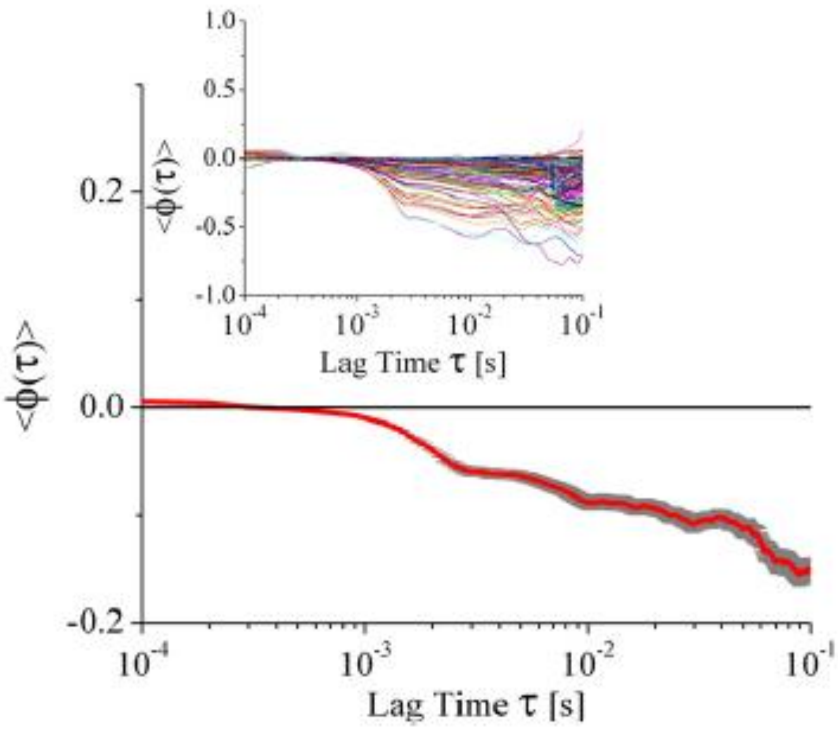
Anti-persistent motion

Persistent motion

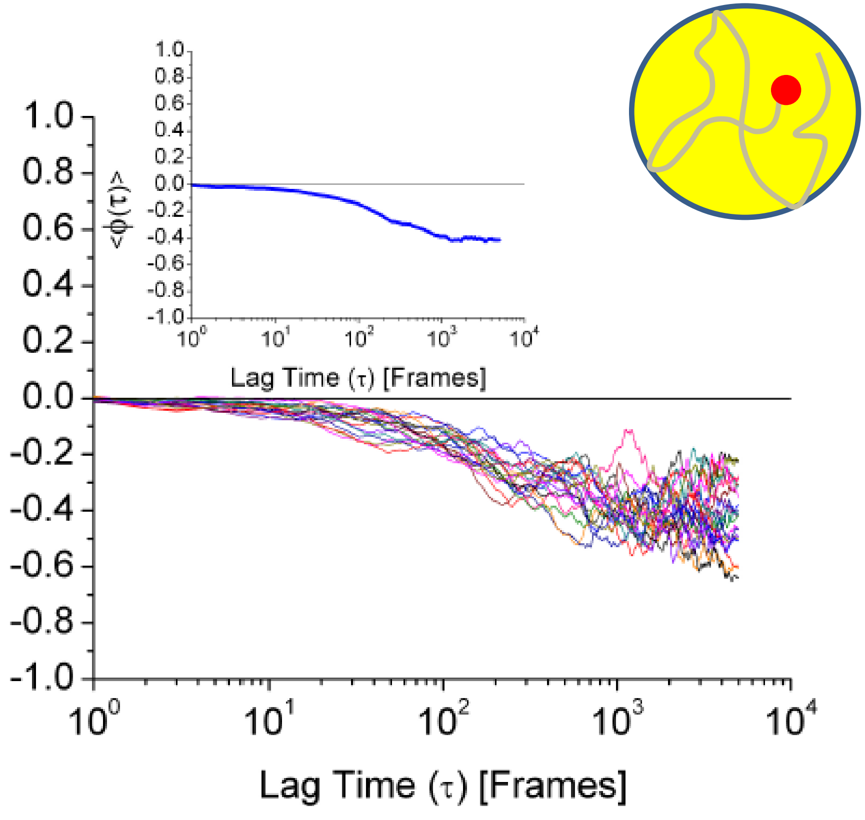
A.W.Harrison, et al, *Physical Biology*, 2013, 10, 36002.
B.Stanislav et al, *PNAS*, 2013, 110, 49, 19689.

Angular correlations without microtubules

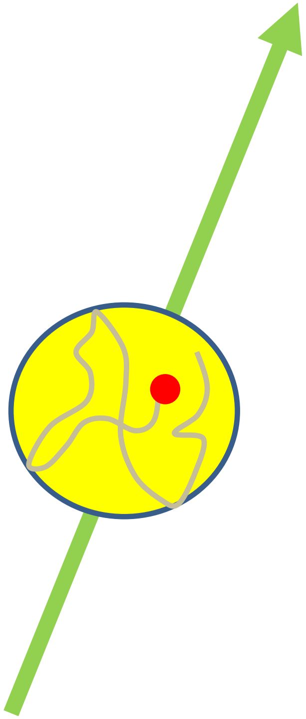
Data

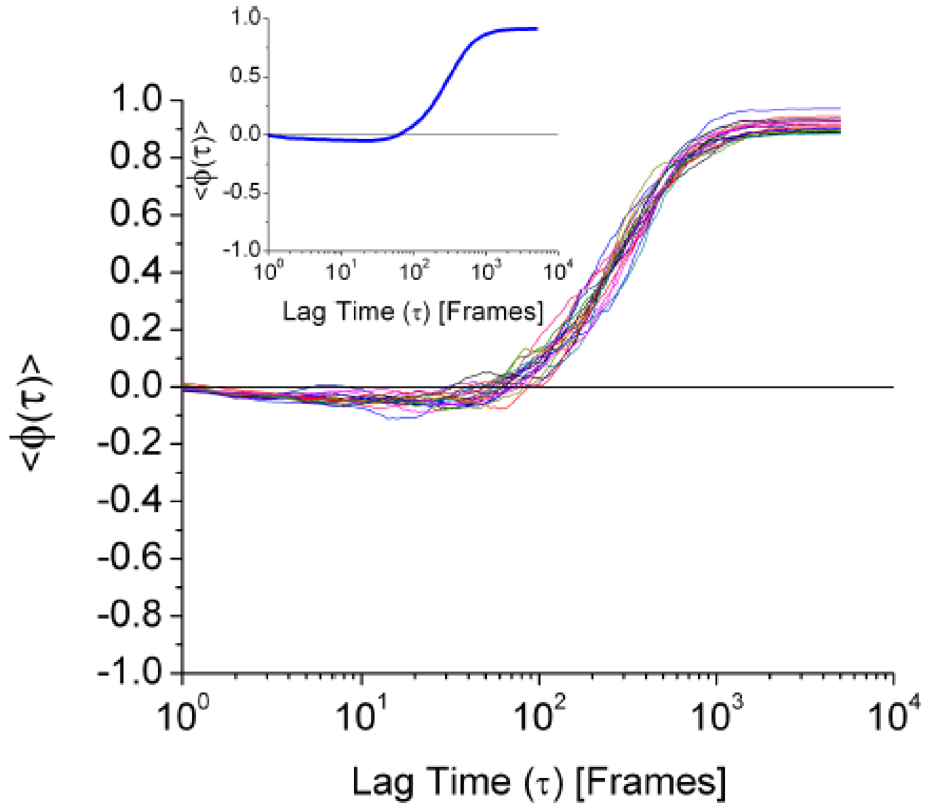


Simulation



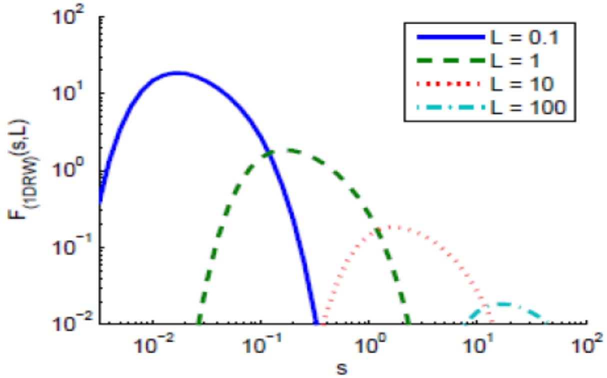
Angular correlations with microtubules: simulations





First passage probability

$$F(s,L) = \frac{\pi D}{L}\sum_{k=0}^{\infty}(-1)^k(2k+1)e^{-\left(\frac{(2k+1)\pi}{2L}\right)\frac{Ds}{L}}$$



Advantages:

Sensitive to a small number of tracks that move over long distances.

Robust representation of data. No smoothing assumptions are made.

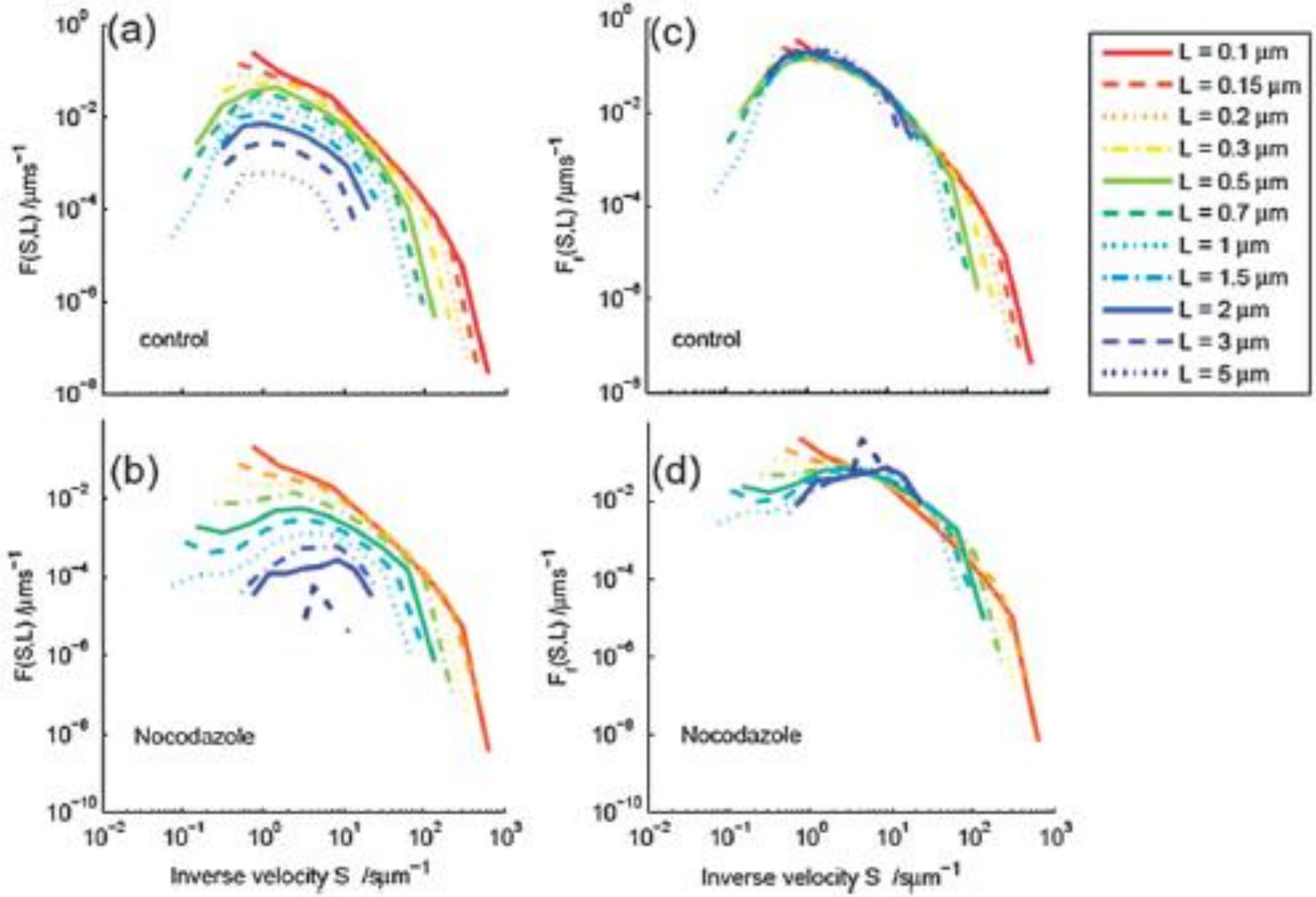
Fits in well with diffusion to reaction type behaviour.

Provides two new results – stretched exponential distribution of vesicle transport lengths and the dependence of vesicle velocity on transport length (different motors are used for different transit lengths?).

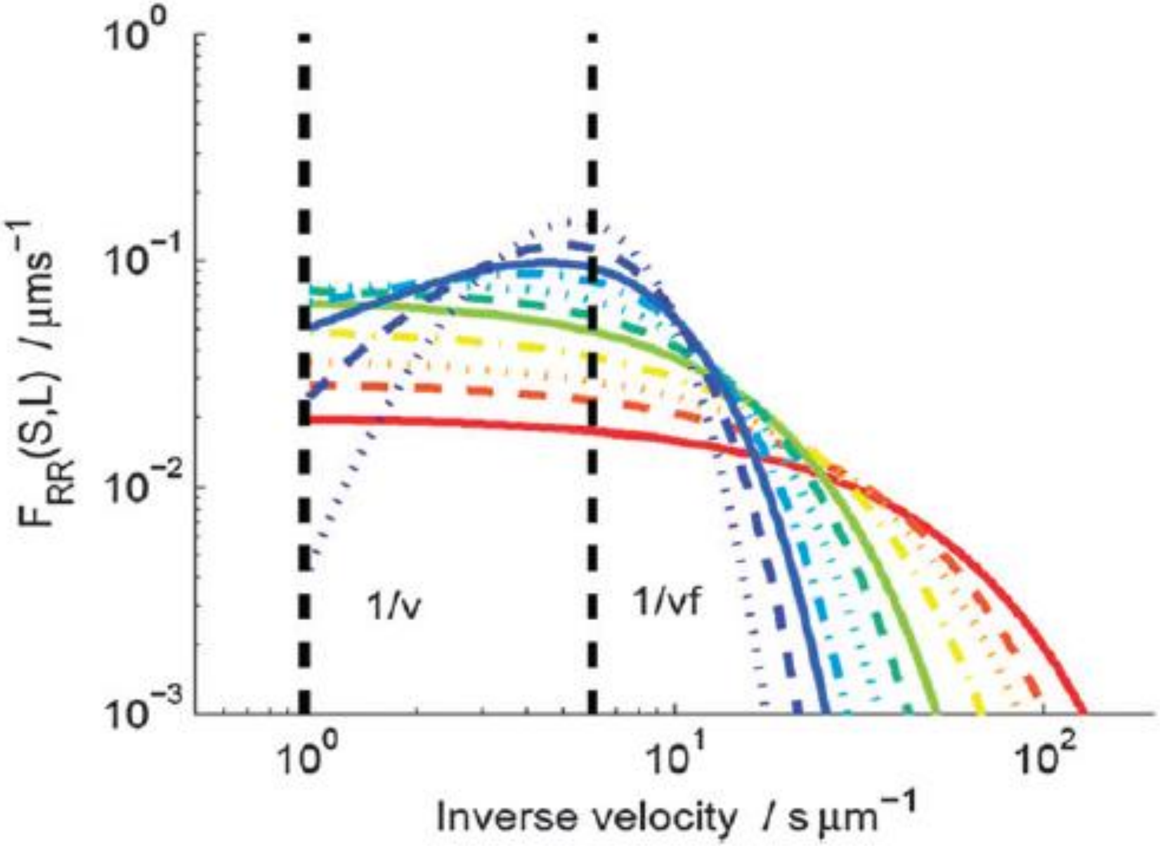
Provides a spatially dependent rate constant that can be used with systems biology modelling.

S.S.Rogers, N.Flores-Rodriguez, V.J.Allan, P.G.Woodman, T.A.Waigh, *PCCP*, 2010, 12, 3753.

FPP for Rab5 transport in live cells



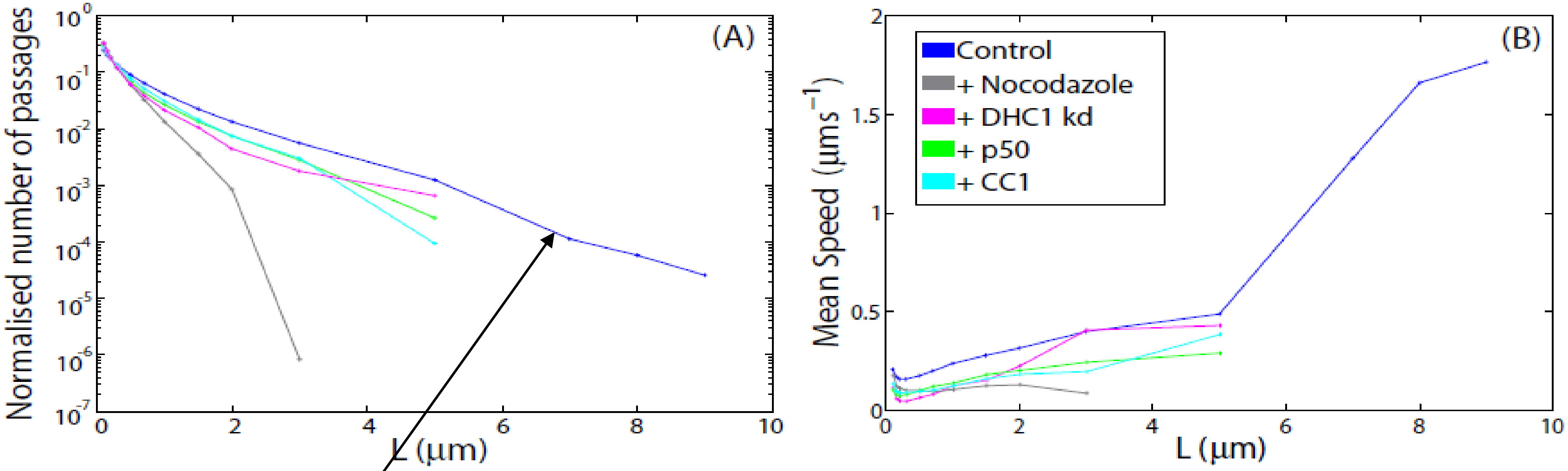
Analytic model for slow FPP



Unidirectional run-rest model.

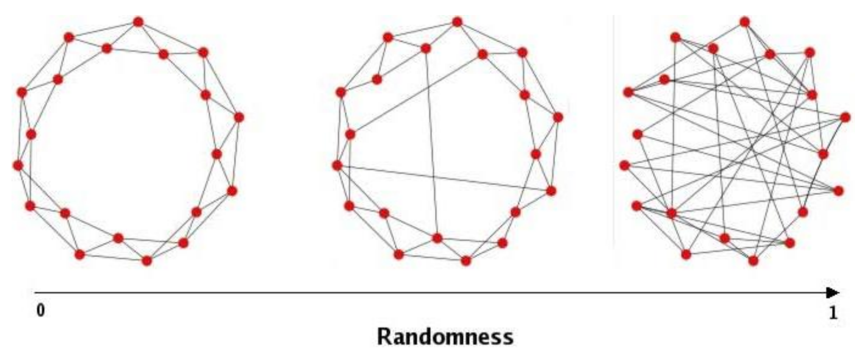
f is the fraction of the time spent running and v is the average velocity.

First passage probability



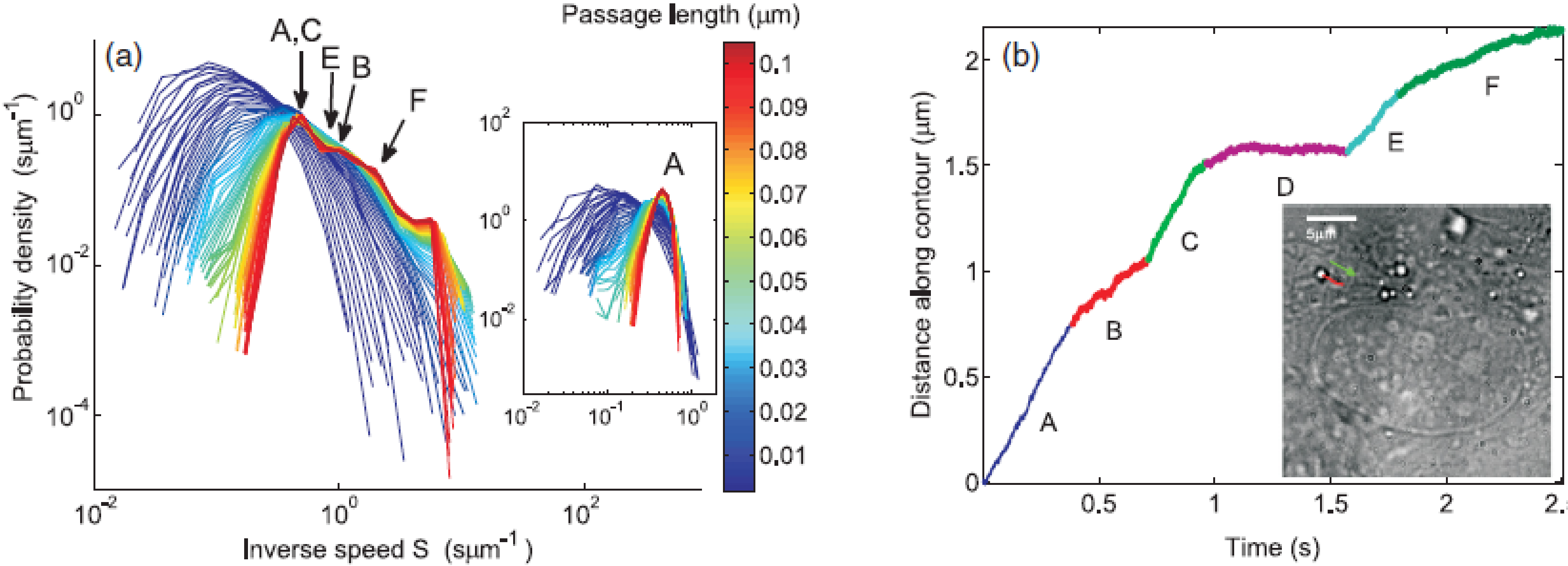
Fat-tailed distribution

French rail system model:
Local transport is slow,
Global transport is fast.
Small world network dynamics?



N.F.Rodriguez, S.S.Rogers, T.A.Waigh, P.G.Woodman, V.J.Allan, *PLoS One*, 2011, 6, 9, e24479.

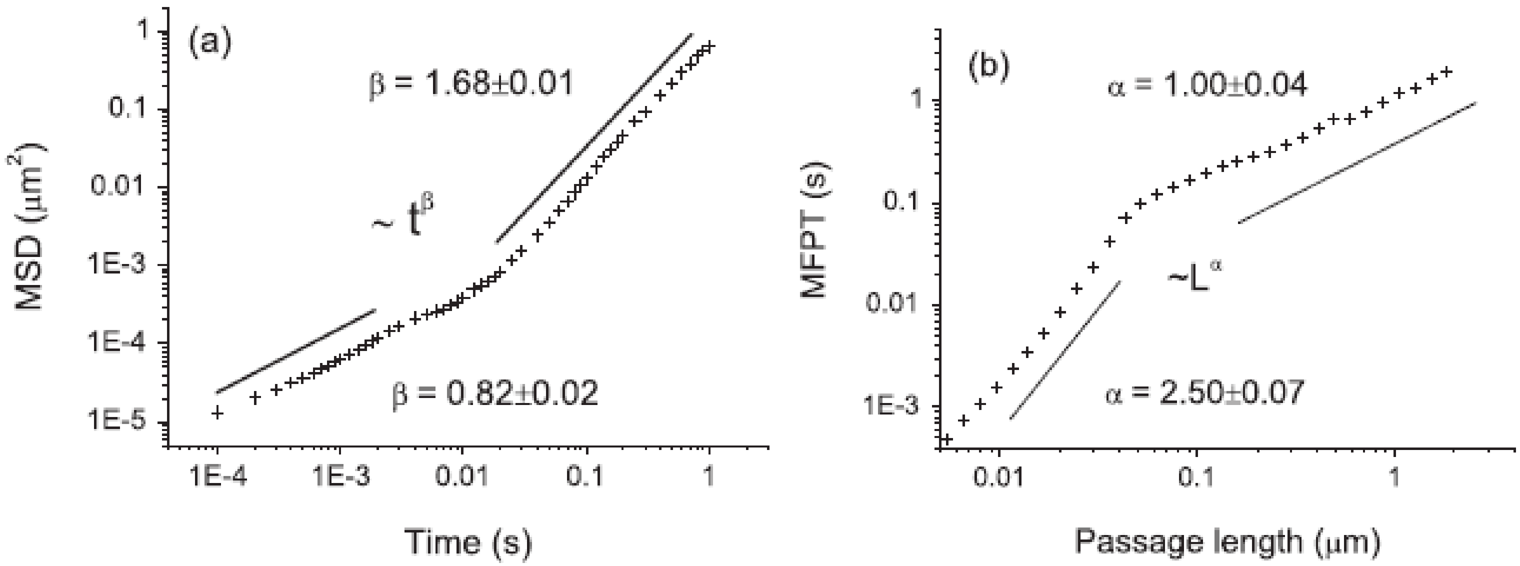
Fast first passage probability



Extract unbiased velocity of runs.

D.A.Kenwright, et al, *Physical Review E*, 2012, 86, 31910.

Mean first passage time



Fractal Brownian Motion

$$\langle r^2 \rangle = MSD \sim t^{1/v} \qquad MFPT \sim L^{2v}$$

Reasonable, but not perfect agreement, walk dimension v=1.21 versus 1.25.

Conclusions

Angular correlation and first passage probabilities are useful underused measures of active motion.

Future work

- Super-resolution fluorescence techniques.
- Stepping motion with a Kalman filter (Bayesian method – need a reasonable guess of the transport dynamics).