九州大学
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Athermal Fluctuations of Probe Particles in Active Cytoskeletal Network

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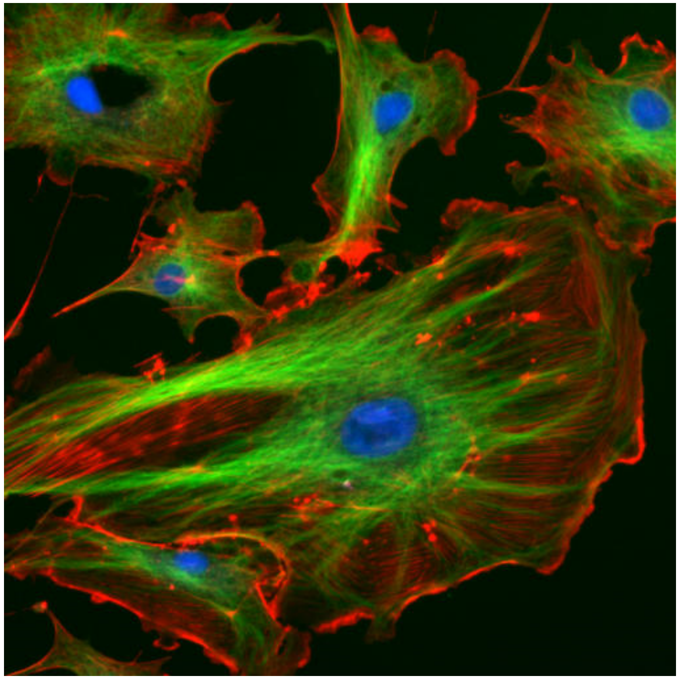
Cytoskeleton

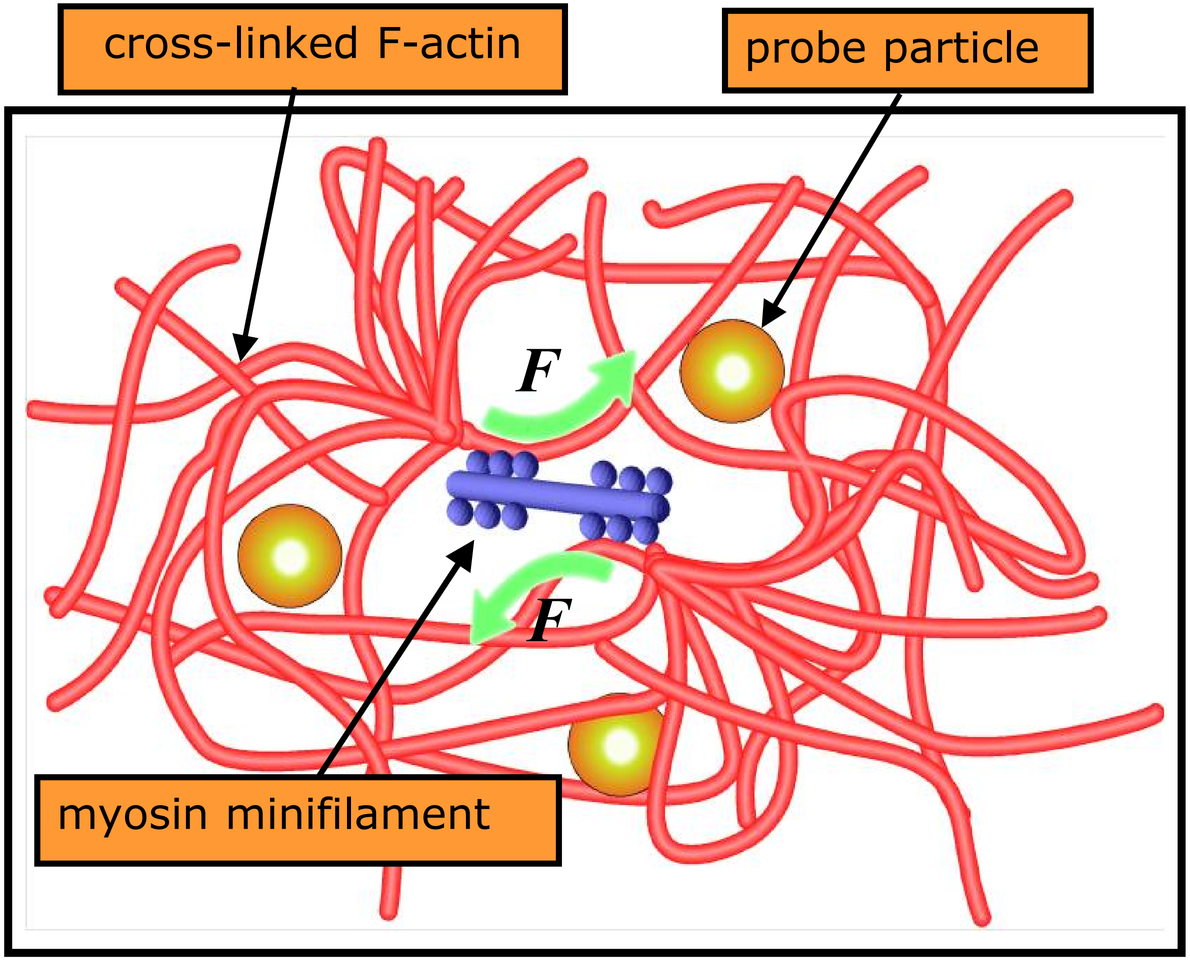
Fluorescent picture of a cell



cytoskeleton		motor proteins
F-actin	⟺	myosin
microtubule	⟺	dynein, kinesin
intermediate filament		- - -

Objective:
To investigate the nonequilibrium statistics and dynamics of actin-myosin network.

Microrheology of Actin-Myosin Network

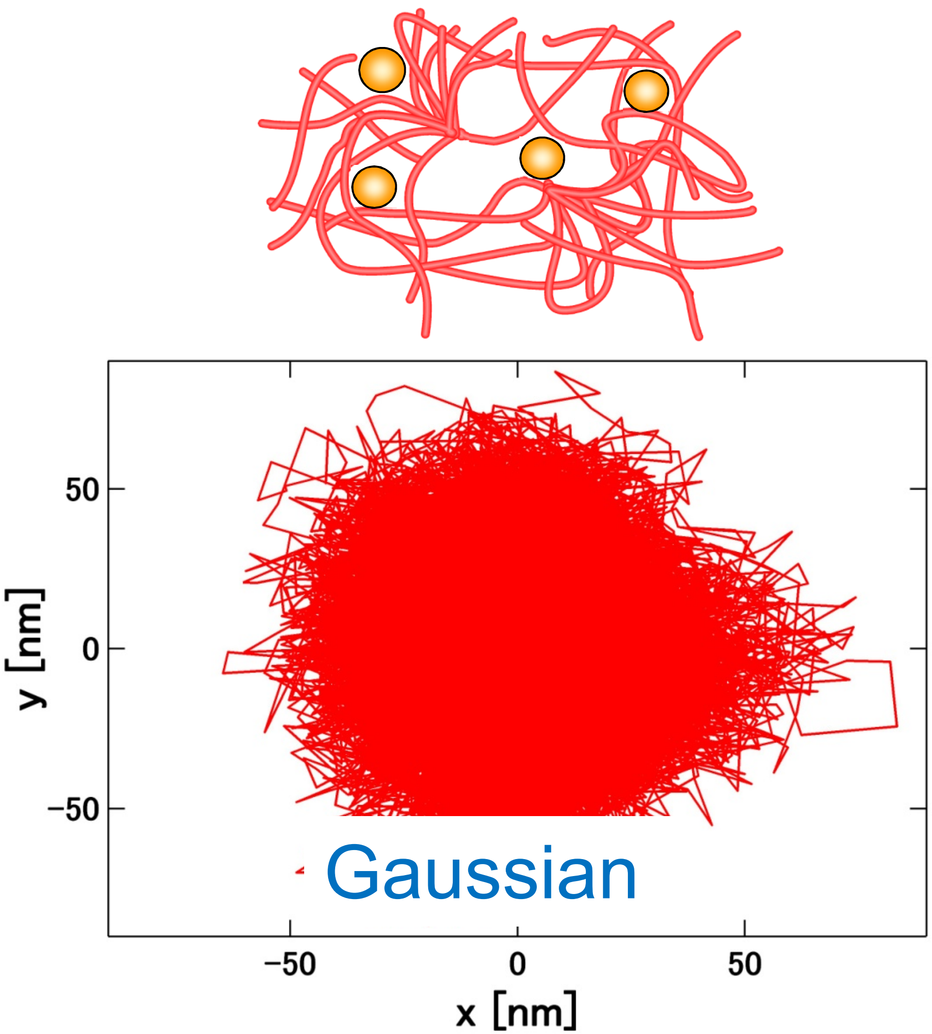


sample chamber (26 mm x 7.0 mm x 0.2 mm)

Particle's trajectory?

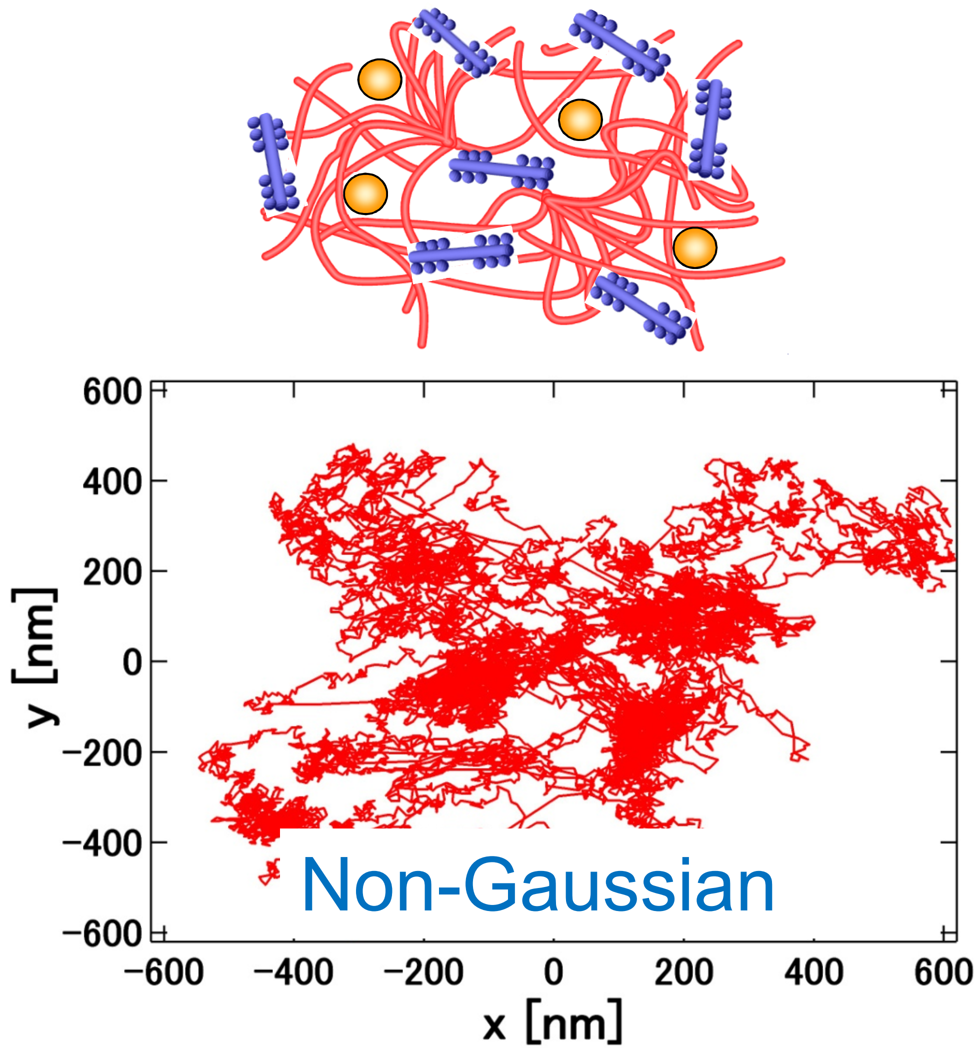
Particles' Trajectories

Actin Network



Passive gel

Actin-Myosin Network

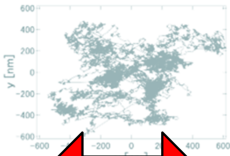


1.0-μm particle; 3.5 mM ATP

Active gel

Motivation

Fluctuations of probe particles in active gel



Non-Gaussian

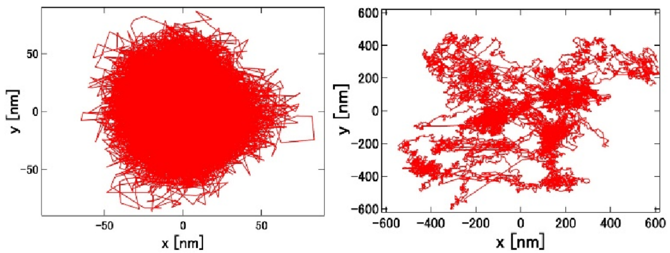
Second Moment Analysis (MSD or PSD)

-won’t tell the exact shape of the distribution

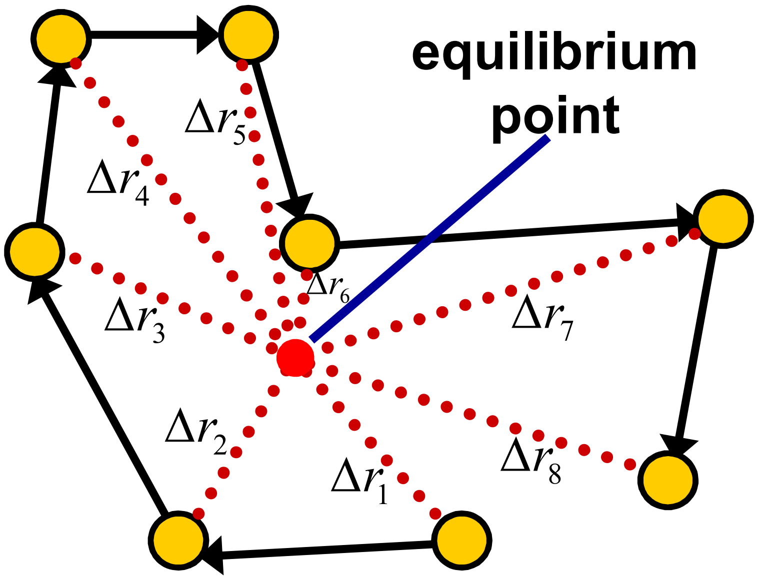
Whole Displacement Distribution

- a model is developed for the displacement distribution in active cytoskeleton

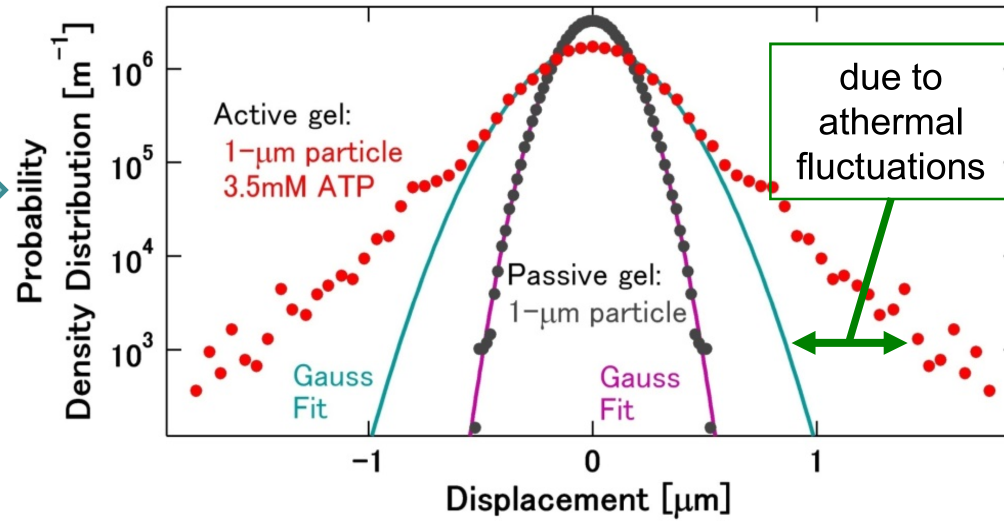
Displacement Distribution



Passive gel **Active gel**



Instantaneous Distribution

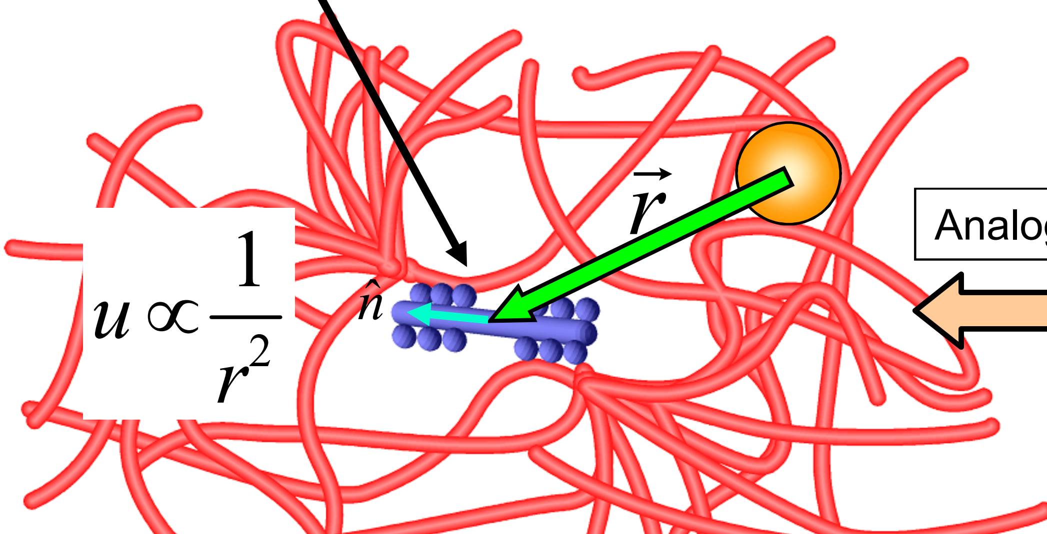


Probability Density Distribution of Δr :

$$P(\Delta r) \rightarrow \text{Instantaneous Distribution (ID)}$$

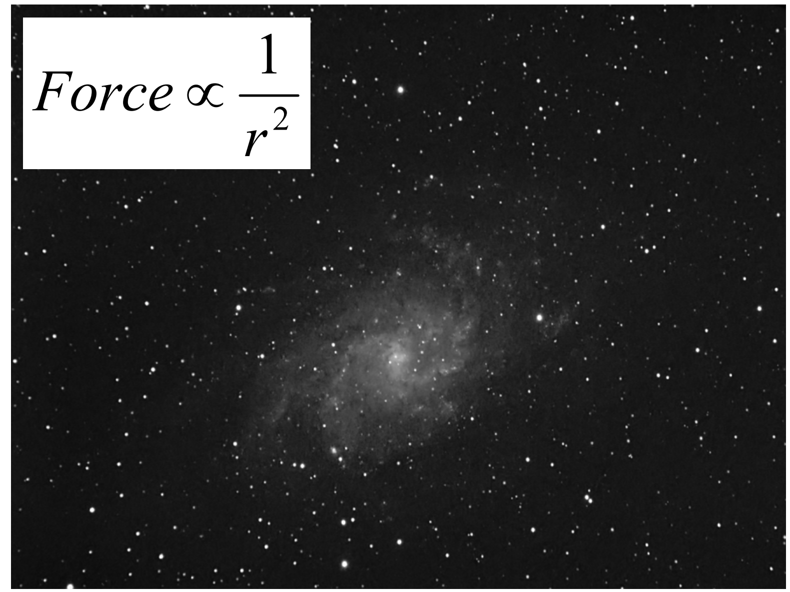
Displacement in Active Cytoskeleton

considered as one force dipole



Analogy

Force distribution in the universe



(Taken from: http://astrophotographia.blogspot.jp/2009/10/m31-andromeda-galaxy.html)

$$\vec{u}(\hat{r},\hat{n}) = \frac{\kappa\{2(1-2\nu)(\hat{r}\cdot\hat{n})\hat{n} - (1-3(\hat{r}\cdot\hat{n})^2)\hat{r}\}}{16\pi\mu(1-\nu)r^2}$$

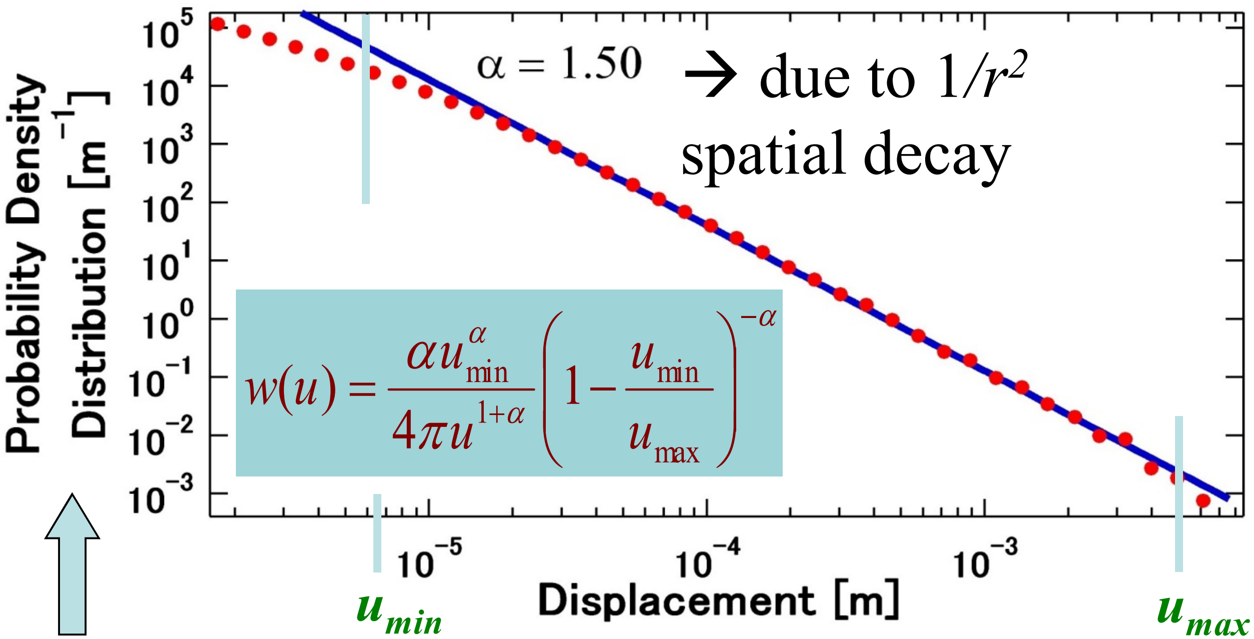
$\vec{u}$: the displacement field of the myosin.
r: the separation between the probe and myosin.
κ: strength of force dipole
μ: elastic modulus

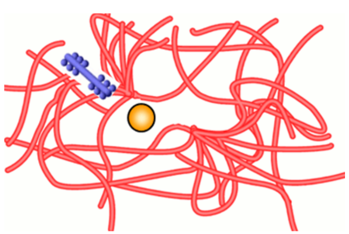
$\hat{r}\cdot\hat{n}$: purely random variable → $w(u) \propto 1/u^{d+\alpha}$

Levy Stable Distribution

$P(F) \propto 1/F^{d+\alpha}$ → $\alpha = 1.5$

Numerical Simulation by I. Zaid

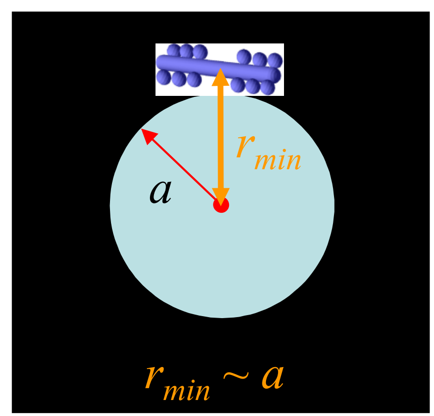


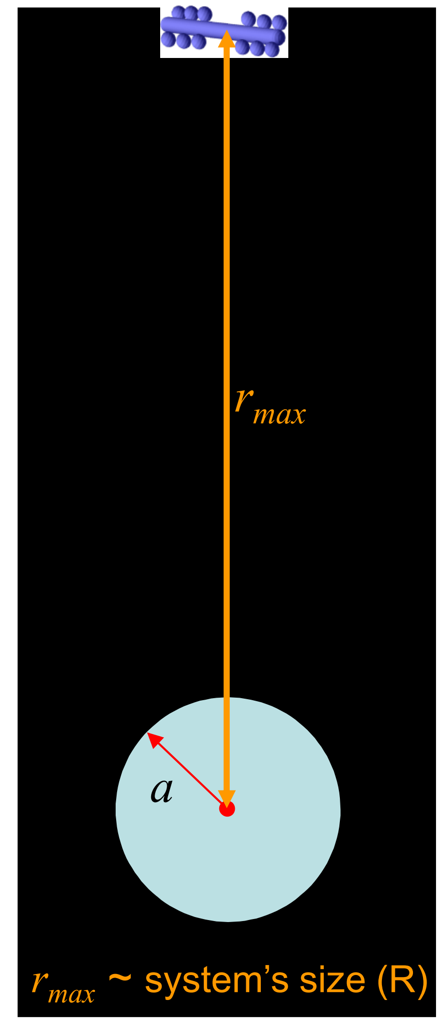


$$u_{\min} \sim \gamma_0 / R^2$$

$$u_{\max} \sim \gamma_0 / a^2$$

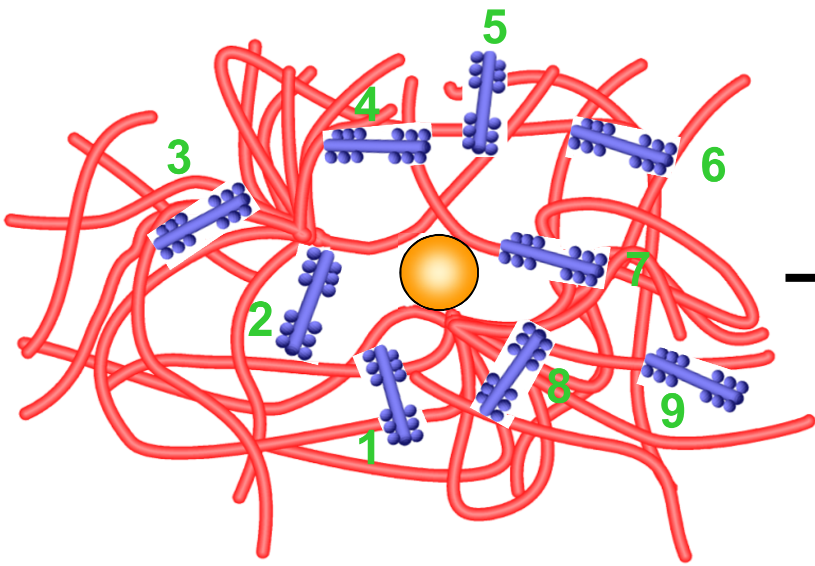
$$\gamma_0 \equiv \kappa / \mu$$





γ_0 : effective mysosins' strength

Model extended for N myosins



Each myosin has independent effect on the particle.

So, the probability density $W(u)$ is an N-fold convolution of

$$w(u) = \frac{\alpha u_{\min}^{\alpha}}{4\pi u^{1+\alpha}}\left(1 - \frac{u_{\min}}{u_{\max}}\right)^{-\alpha}$$

in real space:

$$W(u,N) = \int_{-\infty}^{\infty} du_1 w_1(u_1) \ldots du_{N-1} w_{N-1}(u_{N-1}) \ldots w_N\left(u - \sum_{i=1}^{N-1} u_i\right)$$

(in Fourier space)

$$W(k) = w(k)^N$$

Fourier Transform:

$$\Im(w(u)) = w(k) = \int e^{iuk} w(\mathbf{u}) d^3 u$$

The probability density function due to N myosins (in Fourier space calculation)

$$W(k)_{ID} = e^{ca^3\left[1 - {}_3F_2\left(\frac{1}{2}, 1, -\frac{\alpha}{2}; \frac{d}{2}, 1-\frac{\alpha}{2}; -\frac{\gamma_0{}^2 k^2}{a^4}\right)\right]}$$

$$N\left(\frac{u_{\min}}{u_{\max}}\right)^{\alpha} \approx ca^3$$

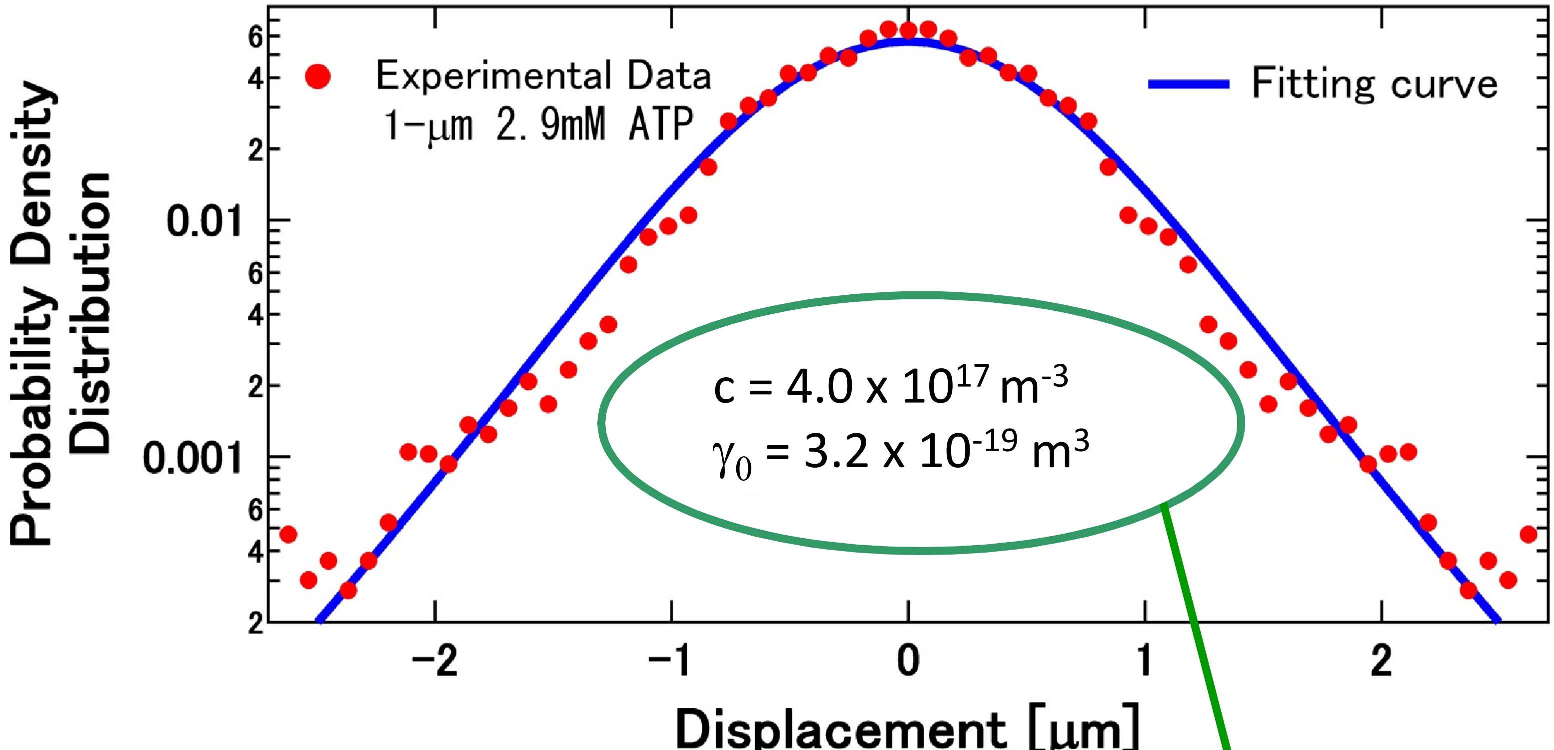
Mathematical Model for Instantaneous Distribution

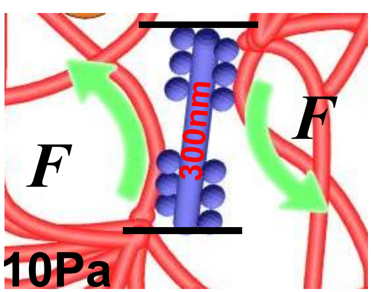
c is the effective concentration of myosins,

a is the radius of the probe particle, ${}_3F_2$ is the hypergeometric function,

and γ_0 indicates the myosin's strength.

ID for Active Gel and the fitting curve





consistent to experimental conditions:

c ~ [1 active myosin aggregate/1 μm^3] ~ 10^{18}

γ_0 ~ [((F=10pN)x 300nm)/10Pa] ~ 10^{-19}

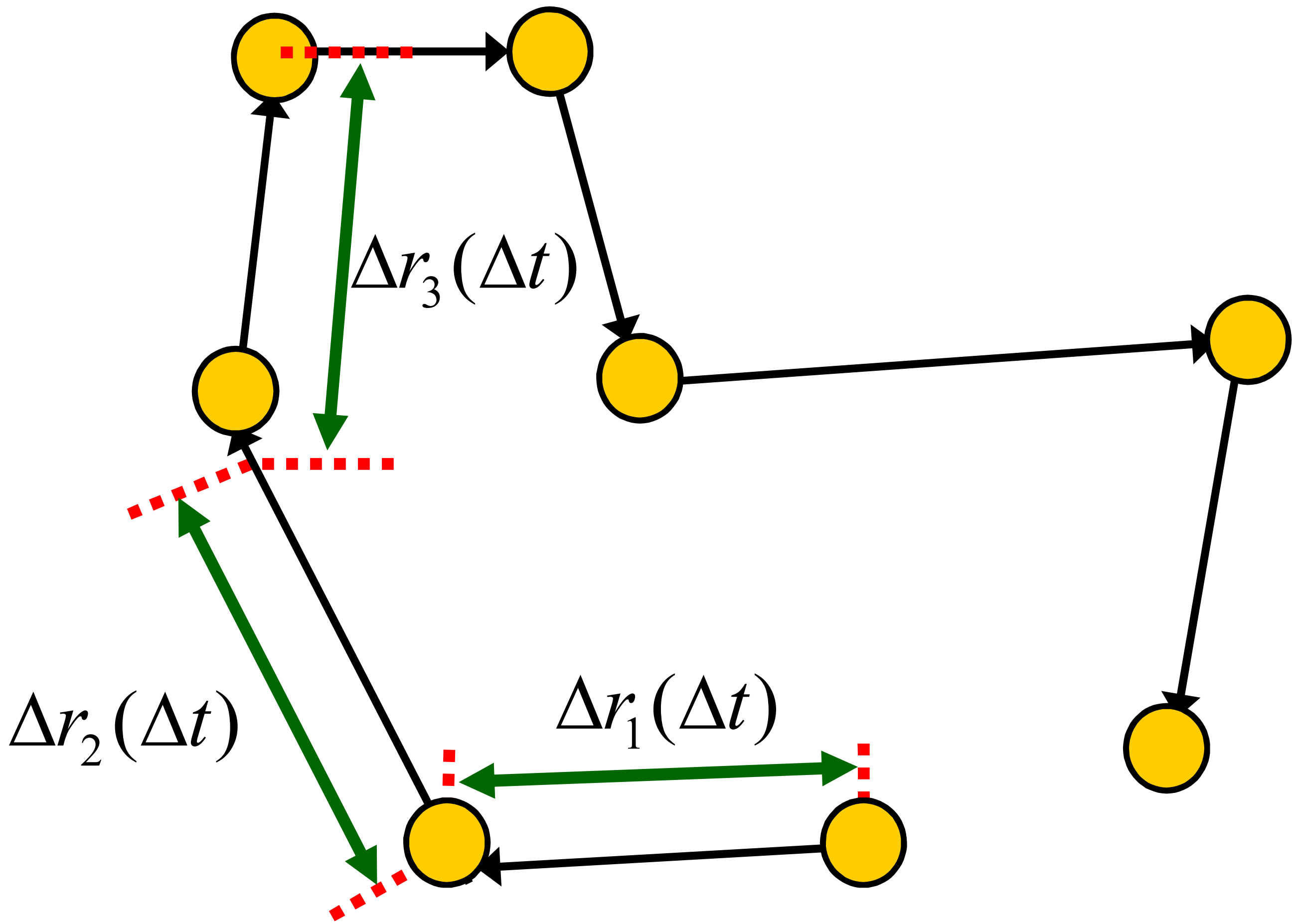
For 1.0-μm particle at 2.9 mM ATP concentration. *c* is the effective myosin concentration and γ_0 indicates the myosin's strength.

The Dynamics of the Fluctuations

Van Hove Distribution (VHD)

Strength rate of the force dipole

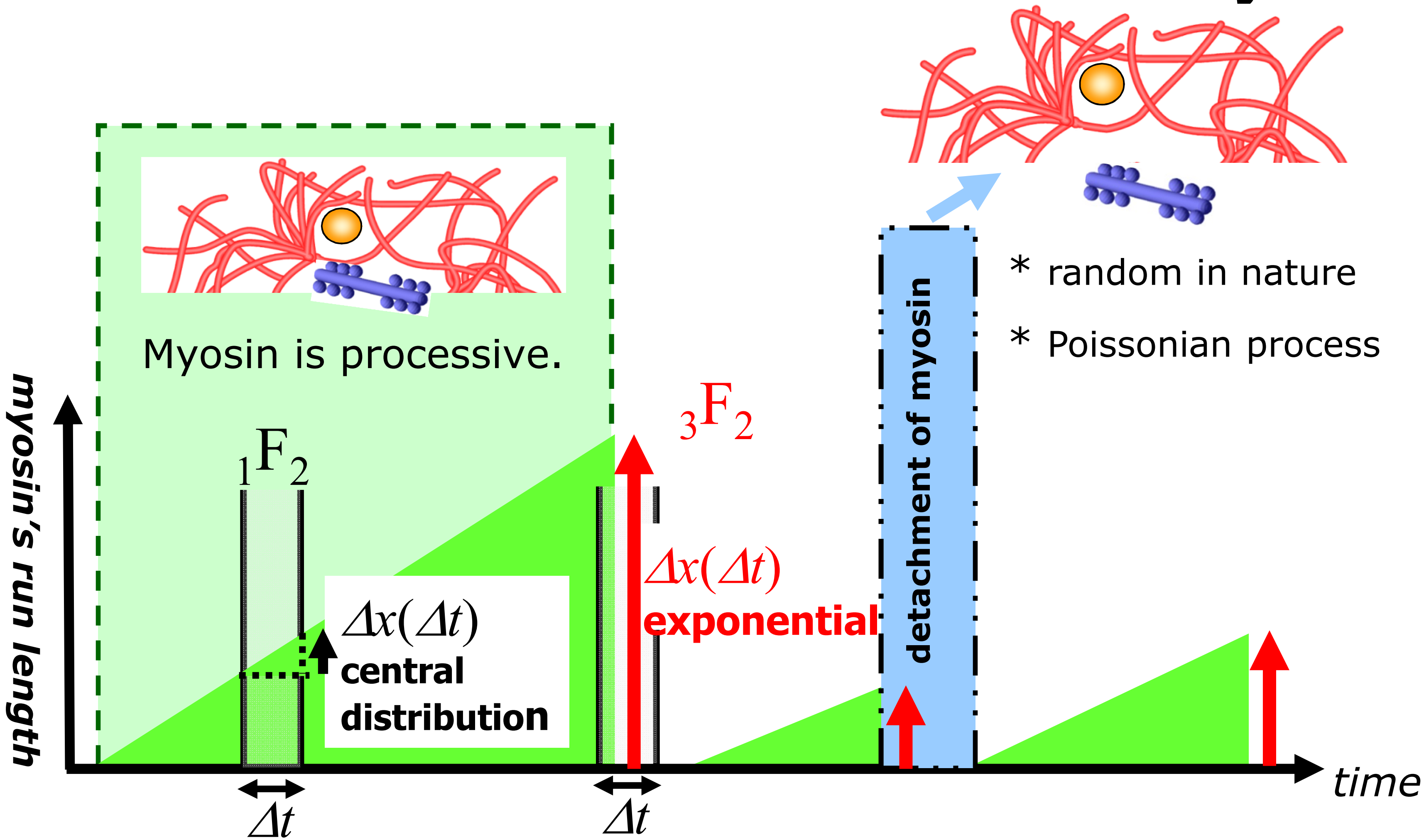
Displacement Distribution



Probability Density Distribution of $\Delta r(\Delta t)$:

$P(\Delta r(\Delta t)) \quad \rightarrow \quad$ van Hove Distribution (VHD)

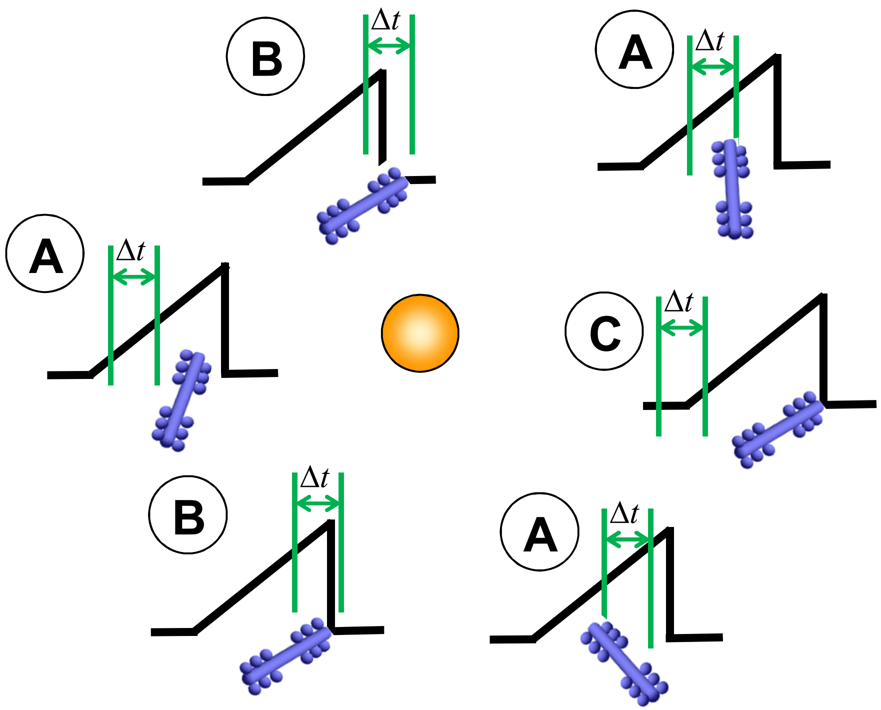
Interaction between Actin and Myosin



$$W(k) = \exp\left[\left\{2-\exp\left(-\frac{\Delta t}{\tau}\right)\right\} ca^3 \left\{1 - \frac{\exp(-\Delta t/\tau)}{2-\exp(-\Delta t/\tau)} {}_1F_2 - \frac{1-\exp(-\Delta t/\tau)}{2-\exp(-\Delta t/\tau)} {}_3F_2\right\} - ca^3\left\{\frac{1}{\tau}\int_0^{\Delta t} {}_1F_2 \exp\left(-\frac{\Delta t'}{\tau}\right) d\Delta t'\right\}\right] \times \exp\left[c_m a^3 (\Delta t/\tau)\left\{1 - {}_1\hat{F}_2\right\}\right]$$

$${}_1F_2 \equiv {}_1F_2\left(-\frac{\alpha}{2};\frac{d}{2},1-\frac{\alpha}{2};-\frac{(\dot{\gamma}\Delta t)^2 k^2}{4a^4}\right),\quad {}_3F_2 \equiv {}_3F_2\left(\frac{1}{2},1,-\frac{\alpha}{2};\frac{d}{2},1-\frac{\alpha}{2};-\frac{{\gamma_0}^2 k^2}{a^4}\right),\quad {}_1\hat{F}_2 \equiv {}_1F_2\left(-\frac{\alpha}{2};\frac{d}{2},1-\frac{\alpha}{2};-\frac{(\gamma_m \Delta t)^2 k^2}{4a^4}\right)$$

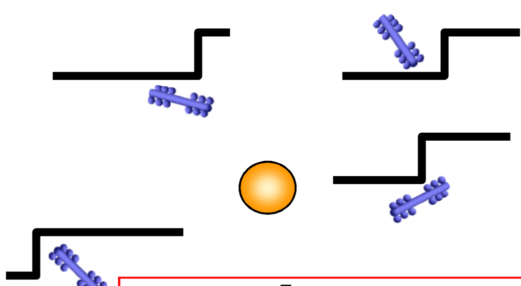
Visualization of the hypergeometric function terms



A
$$W(k)=e^{ca^3[1-{}_1F_2]}$$

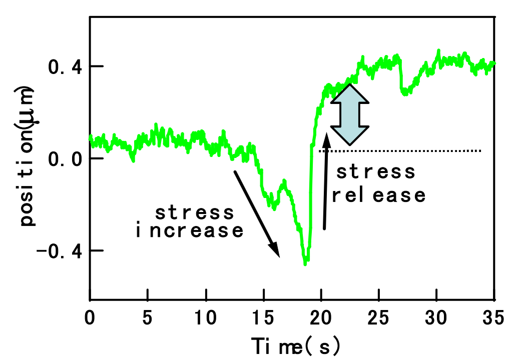
B
$$W(k)=e^{ca^3[1-{}_3F_2]}$$

C
$$W(k)=e^{-ca^3/\tau\int_0^{\Delta t}{}_1F_2\exp(-\Delta t'/\tau)d\Delta t'}$$

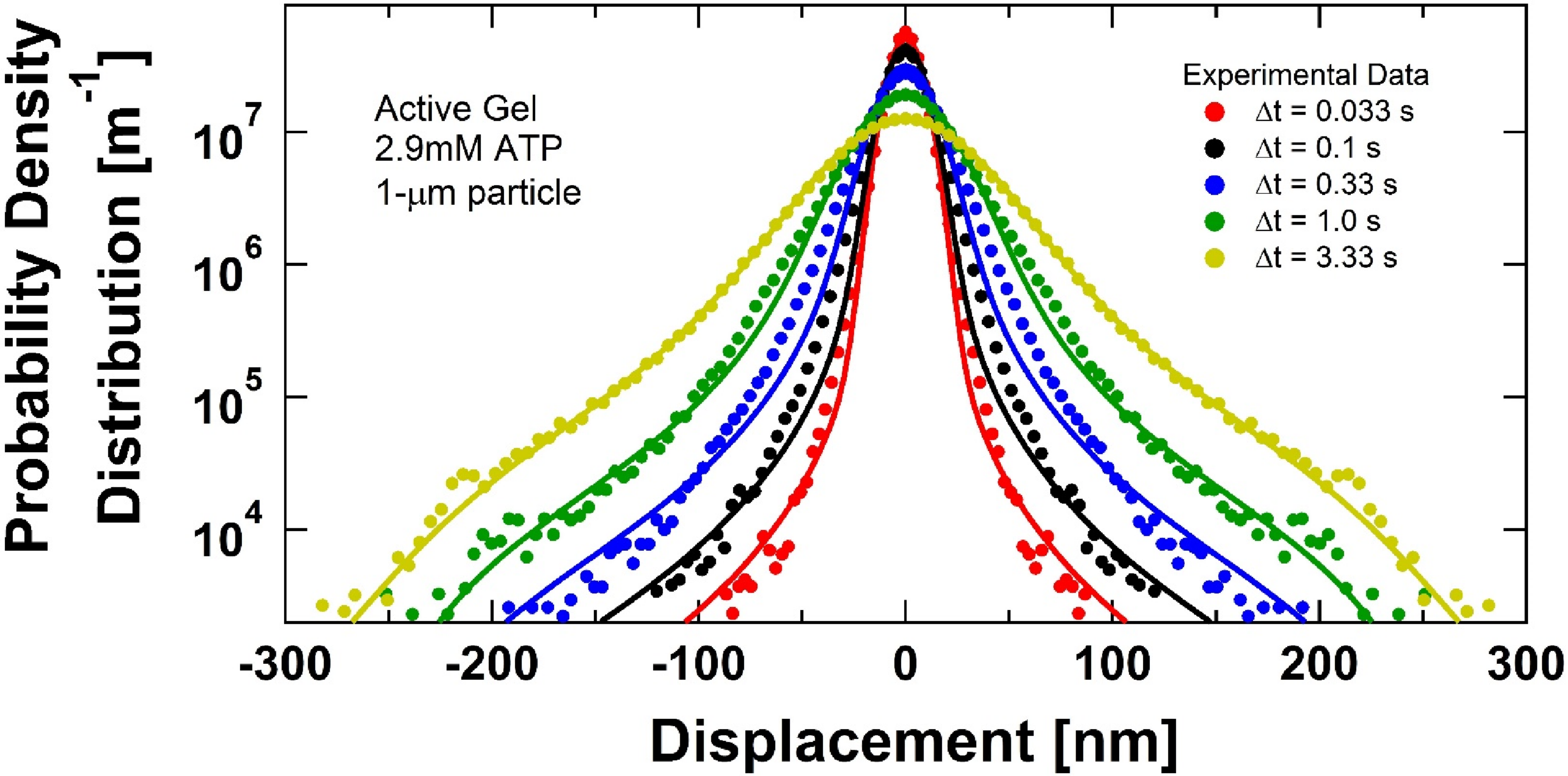


$$W(k)=\exp\left[c_m a^3\left(\Delta t/\tau\right)\left\{1-{}_1\hat{F}_2\right\}\right]$$

$${}_1\hat{F}_2 \equiv {}_1F_2\left(-\frac{\alpha}{2};\frac{d}{2},1-\frac{\alpha}{2};-\frac{\gamma_m{}^2k^2}{4a^4}\right)$$



Van Hove Distribution with fitting curves



Parameter values :

$c = 8.0 \, x \, 10^{17} \ m^{-3}$ $\qquad$ $c_m = 0.6 \, x \, 10^{17} \ m^{-3}$

$\dot{\gamma} = 7.0 \, x \, 10^{-19} \ m^3/s$ $\qquad$ $\gamma_m = 6.0 \, x \, 10^{-20} \ m^3/s$

$\tau = 1.2 \ s$

Conclusion

- The developed model can described well the experimental data.

- Fitting parameter values are consistent with the experimental conditions.

Prospective Work

- Investigation of how the athermal fluctuations of probe particles in cells related to active cytoskeletal network.

Thank you for your attention.