Particle Fluctuations in Ion Channels

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AMSURE 2021

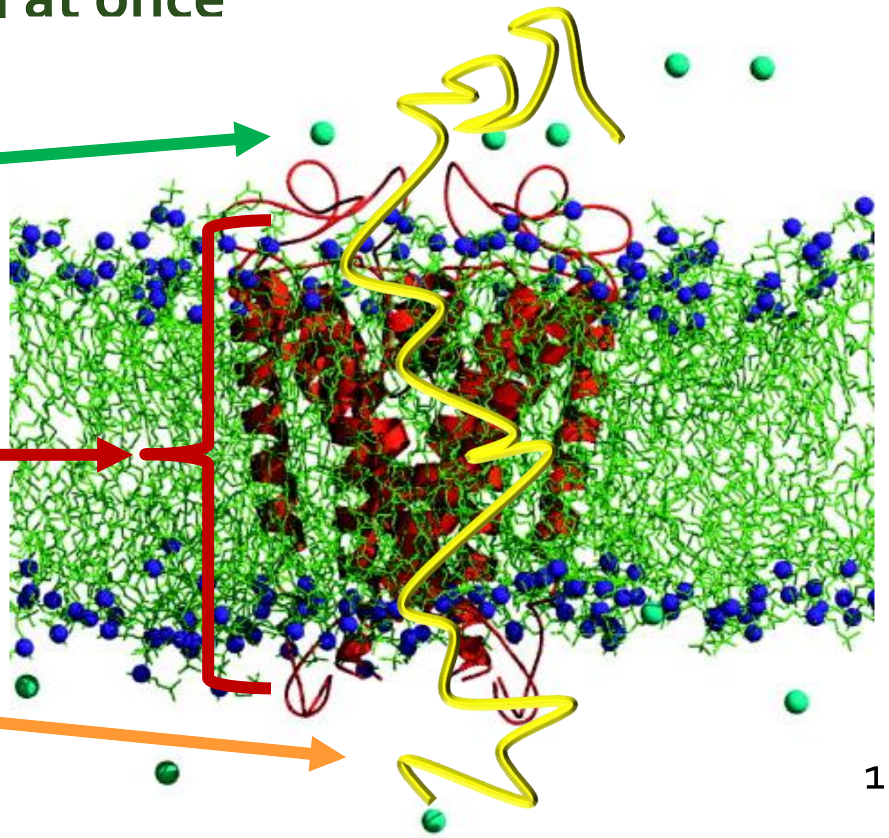
Background

Particles undergo Brownian motion and pass-through Ion channels, with multiple particles being in the channel at once

Particles – Ions such as potassium, sodium, calcium, etc.

Ion channels- proteins arranged to allow passage from one side of a cell membrane to another

Brownian motion- random fluctuations in a particle's position in a fluid



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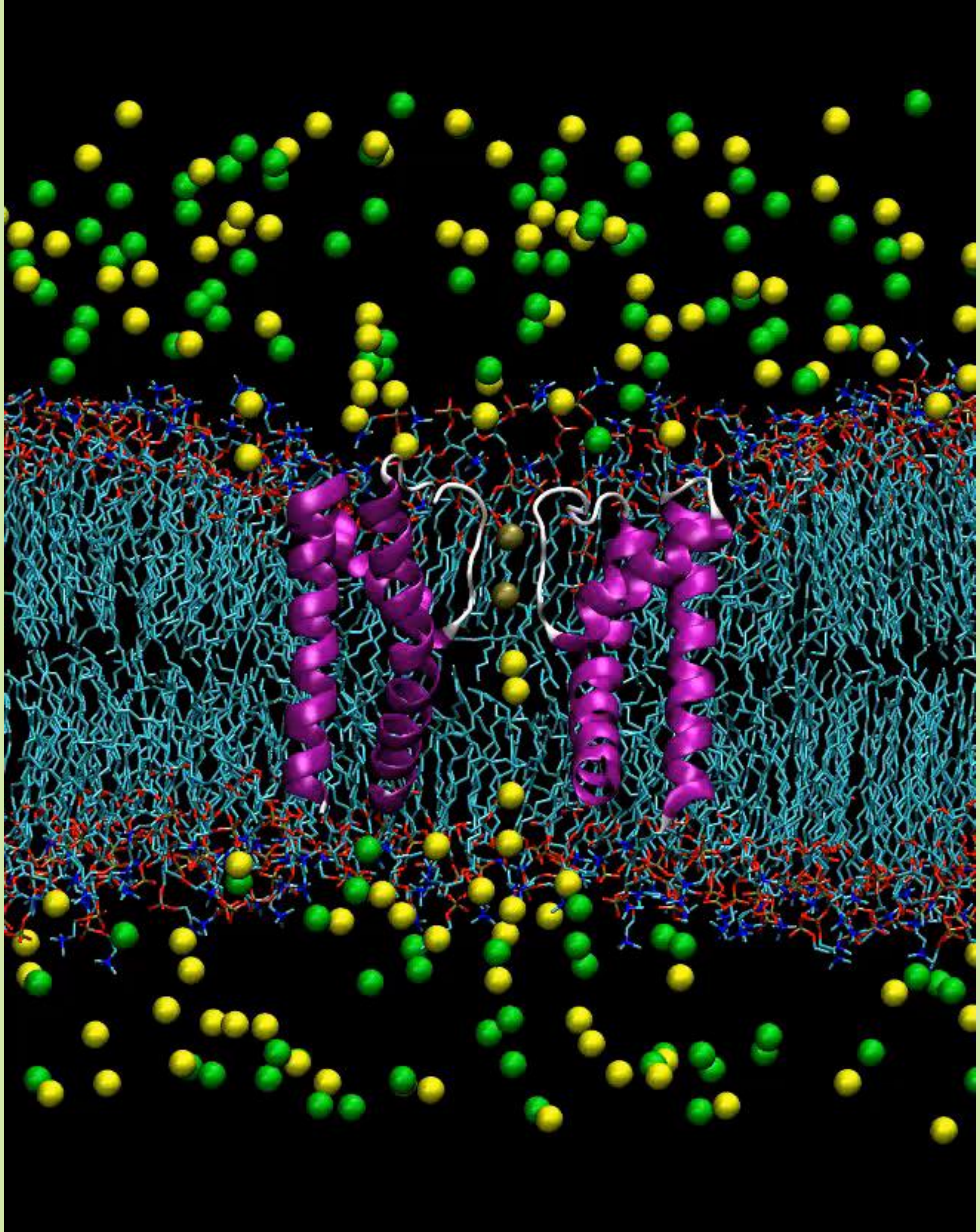
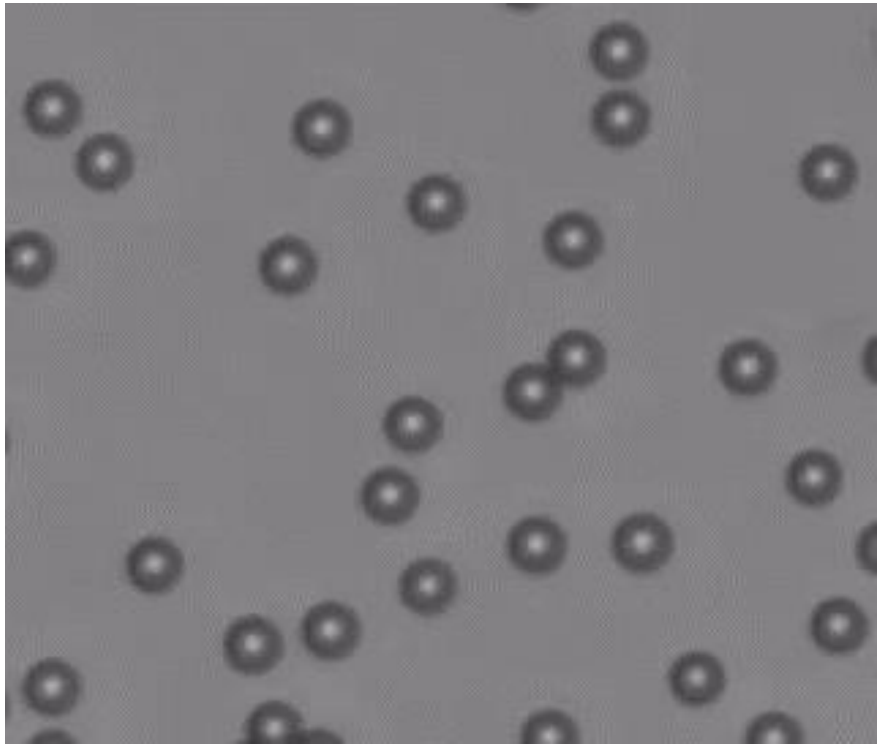
Sansom, M. S. P., Shrivastava, I. H., Ranatunga, K. M., Smith, G. R., Sansom, M. S. P., Shrivastava, I. H., Ranatunga, K. M., & Smith, G. R. (2000). Simulations of ion channels – watching ions and water move. *Trends in Biochemical Sciences*, *25*(8), 368–374.





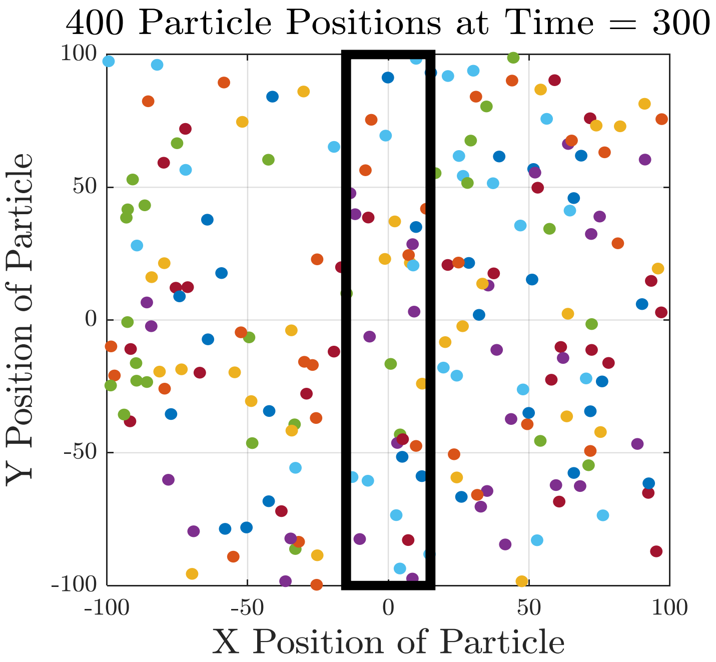
Example of general Brownian Motion

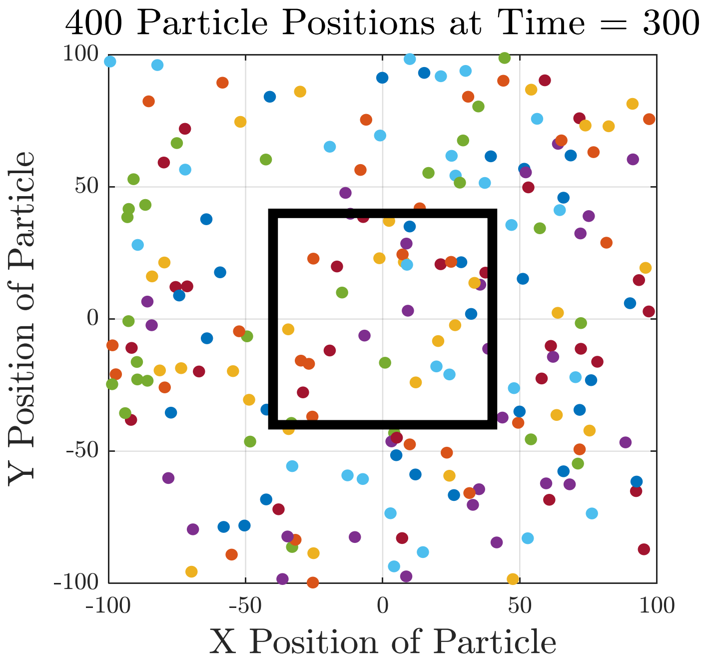
Problem: Difficult to make statistical measurements at a cellular level, and look at the particles inside in the ion channel

Goal: Starting from standard Brownian motion understand how particles are transported through ion channels, specifically how they behave inside the channel

Simulation Set up

- Simulate long particle trajectories in periodic bounded region
- In region there is a box to represent ion channel
- Number of particles in box counted at each time step
- Calculate Mean Squared Displacement(MSD) of **number of particles in the box**

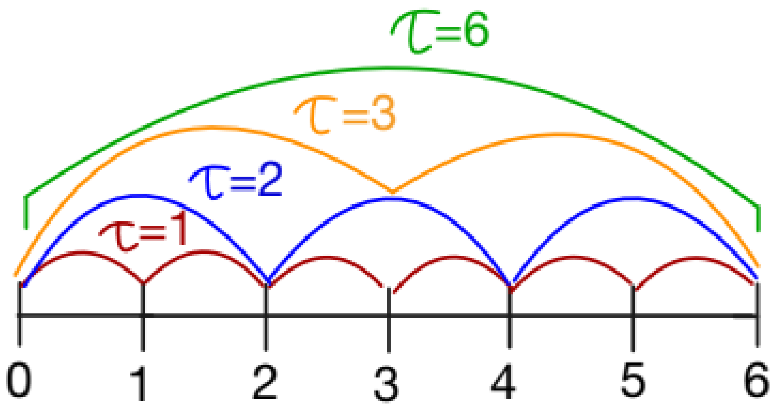




MSD for Brownian Motion

$$MSD(\tau) = \langle \Delta r(\tau)^2 \rangle = \langle [r(t+\tau) - r(t)]^2 \rangle$$

$r(t)$- Particle position at time t



- MSD describes particle movement
- Useful because mean displacement is 0
- Standard Brownian motion has a **linear** MSD

$\langle \Delta r(\tau)^2 \rangle = \frac{2kTd}{\zeta}\tau$, Where $\frac{2kT}{\zeta}$ is a constant, d is dimension

- MSD of number of particles in a box is **not linear**

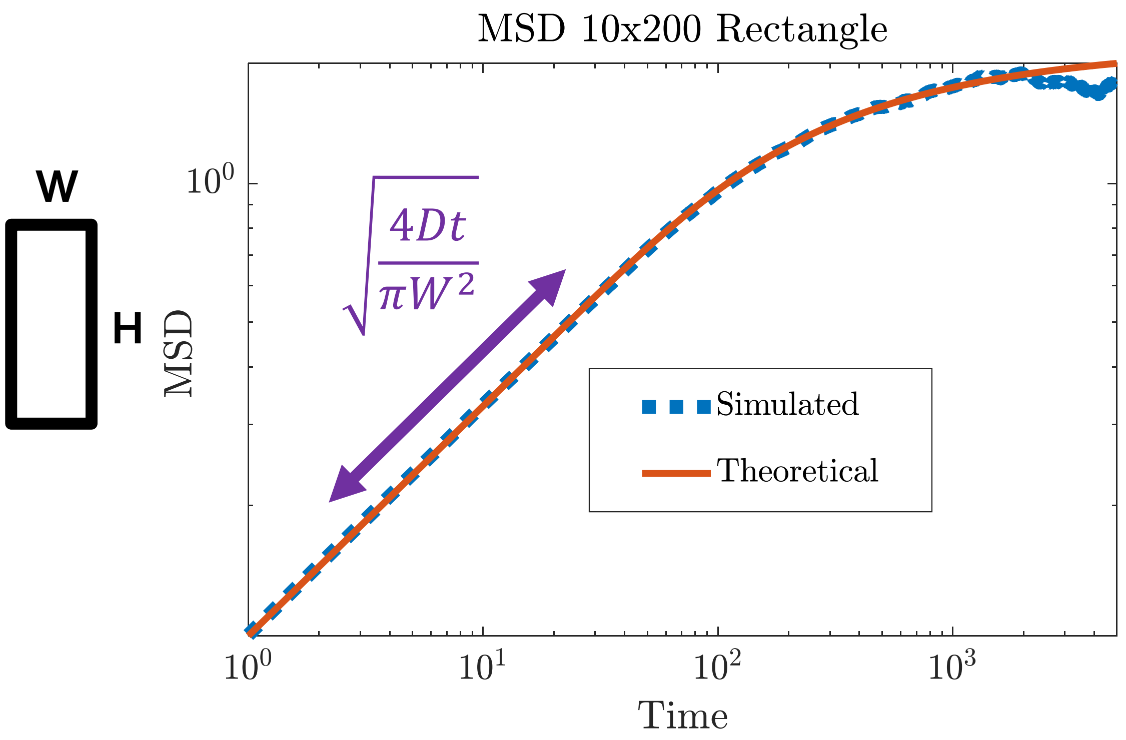
Henry, B. I., Langlands, T. a. M., & Straka, P. (2010). An Introduction to Fractional Diffusion. In *Complex Physical, Biophysical and Econophysical Systems: Vol. Volume 9* (pp. 37–89). WORLD SCIENTIFIC

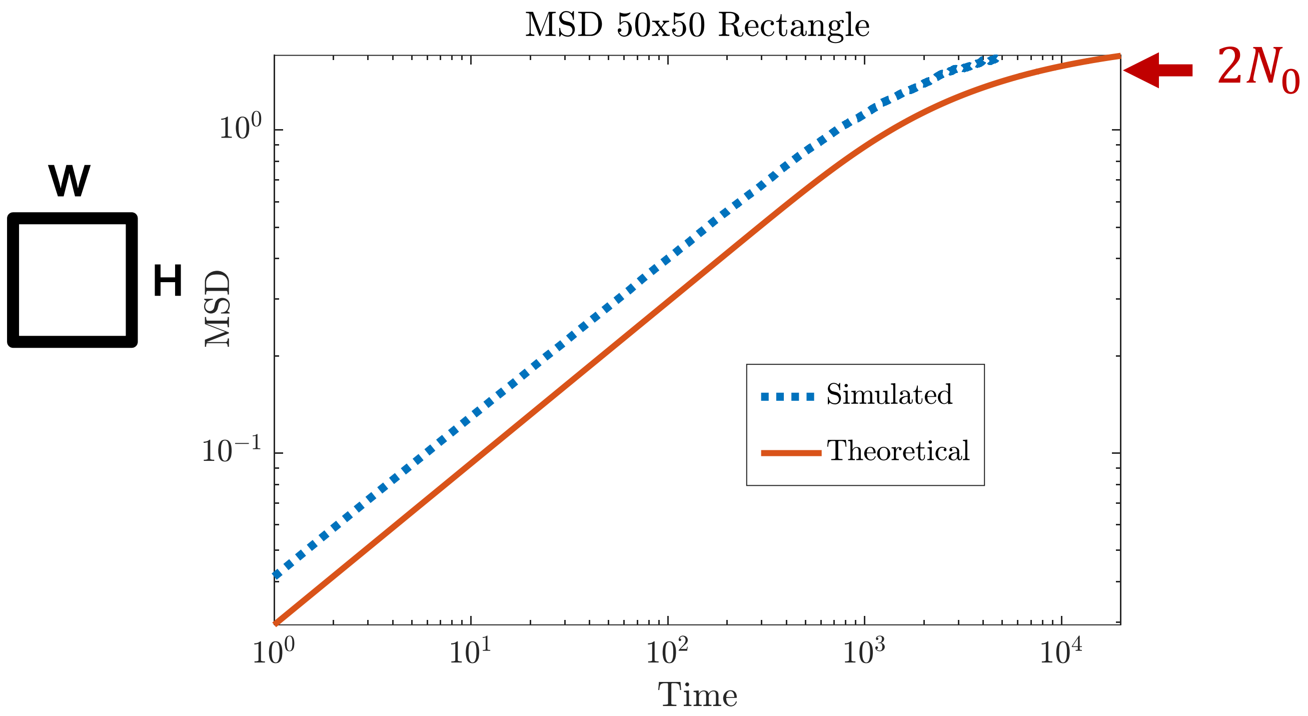
Theoretical MSD

For Number of Particles in the Box

$$\langle (N(t+t_0) - N(t_0))^2 \rangle = 2N_0 \left[\left(1 - e^{-\frac{W^2}{4Dt}}\right) \sqrt{\frac{4Dt}{\pi W^2}} + 1 - \mathrm{erf}\left(\frac{W}{\sqrt{4Dt}}\right) \right]$$

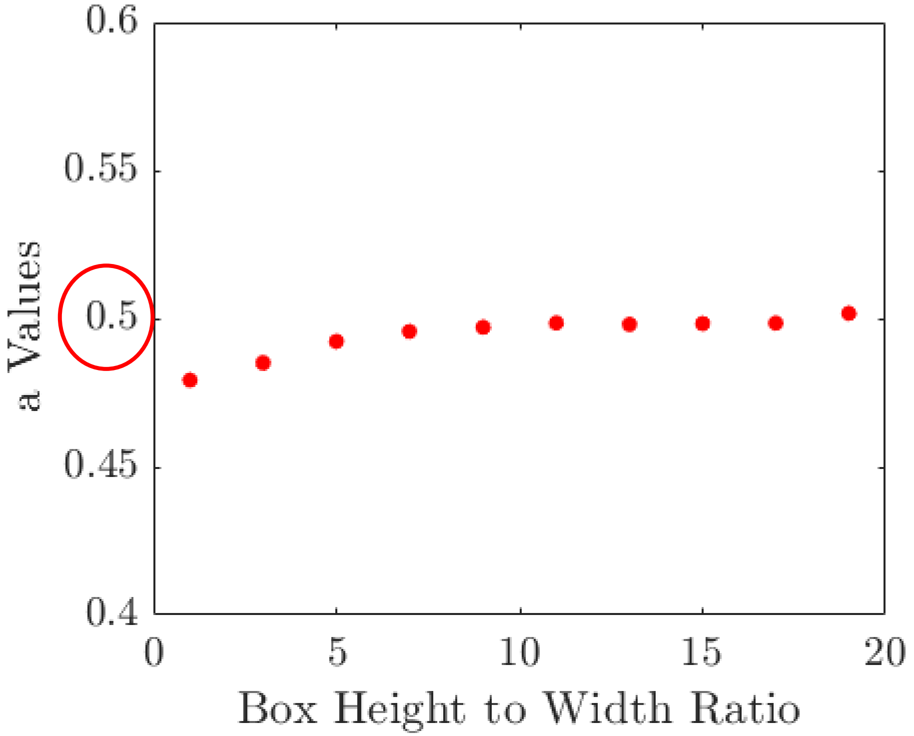
Notation:
$\boldsymbol{N_0}$ - avg. number of particles
$\boldsymbol{W}$ - Width of box
$\boldsymbol{D}$ – Diffusion Coefficient
N$(\boldsymbol{t})$- Number of particles within the box

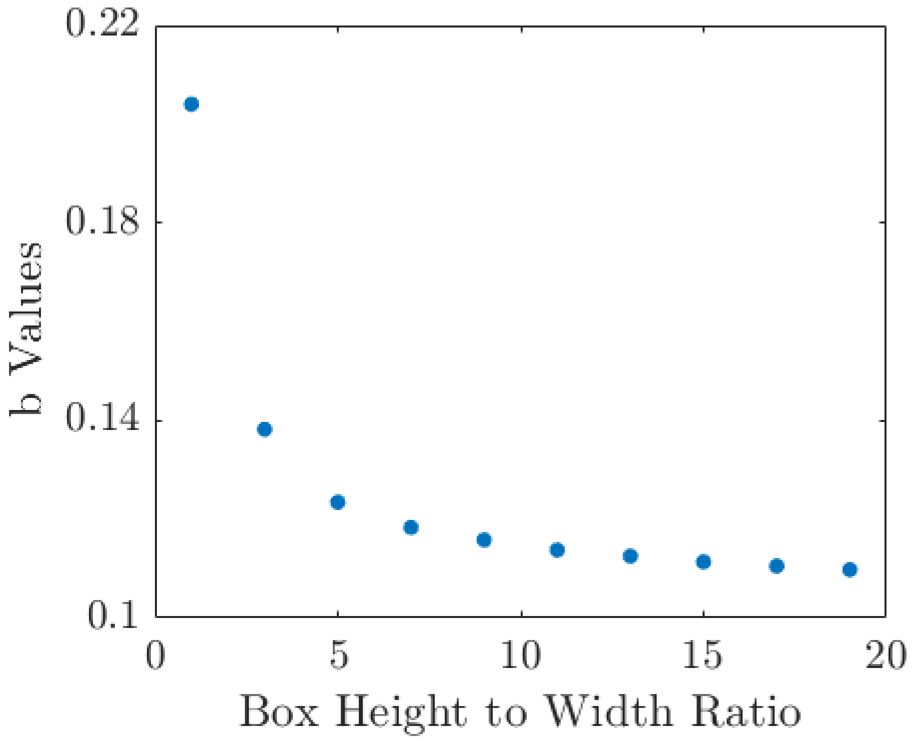




Adjusting Theoretical

- MSD, $\langle N^2(t) \rangle$, fitted to $\boldsymbol{b} \times \boldsymbol{t}^{\boldsymbol{a}}$ for **early times**
  - In both theoretical and simulated $\boldsymbol{a} \approx 0.5$
  - $\boldsymbol{b}$ has various values
  - In theoretical $\boldsymbol{b} = \sqrt{\frac{4D}{\pi W^2}} \approx 0.1$





Adjusting Theoretical

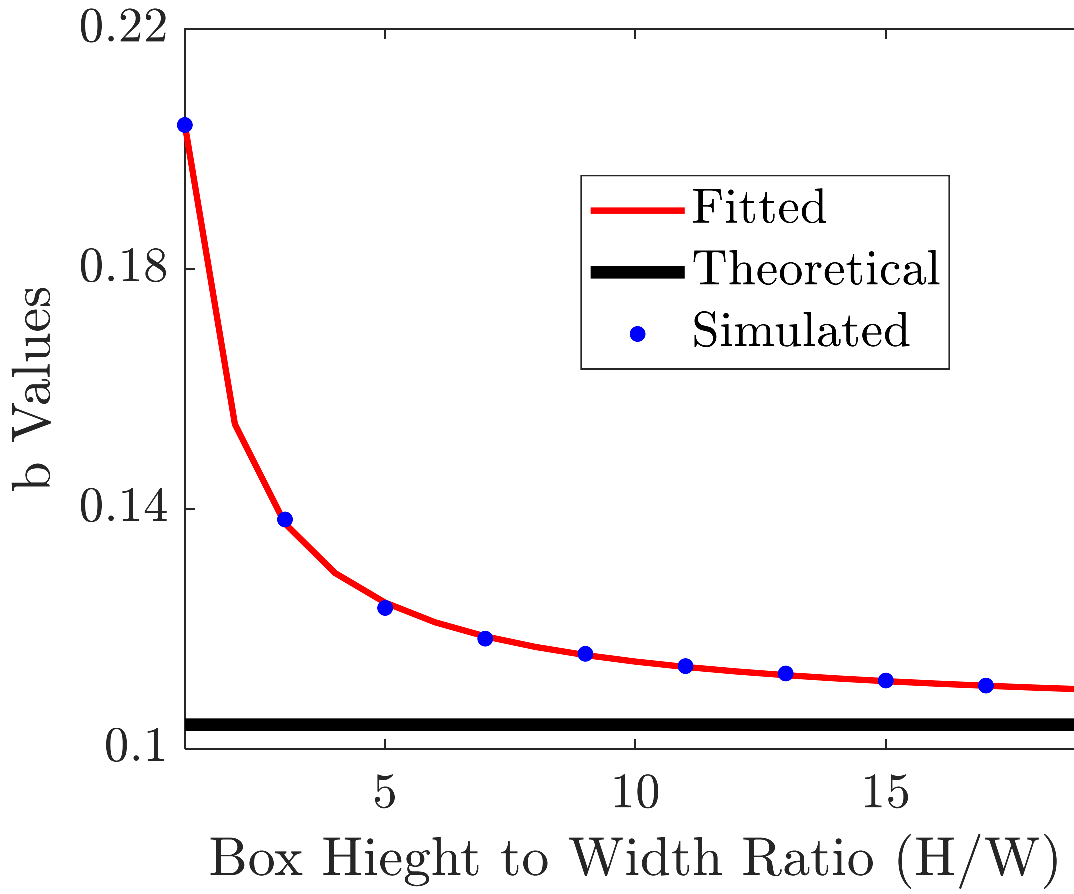
Values of b fitted to $\boldsymbol{c} \times \left(\frac{\boldsymbol{H}}{\boldsymbol{W}}\right)^{\boldsymbol{d}} + \boldsymbol{g}$

$$\boldsymbol{d} \approx -\mathbf{1}$$

$$\boldsymbol{Theoretical}(\boldsymbol{b}_{\infty}) = \boldsymbol{c} = \boldsymbol{g} = \mathbf{2}\sqrt{\frac{\mathbf{4}\boldsymbol{D}}{\boldsymbol{\pi}\boldsymbol{W}^{\mathbf{2}}}}$$

Value of b can be now written as

$$\boldsymbol{b}_{\infty} \times \left(\frac{\boldsymbol{W}}{\boldsymbol{H}} + \mathbf{1}\right) = \frac{\boldsymbol{H} \times \boldsymbol{W}}{\boldsymbol{W} + \boldsymbol{H}}$$



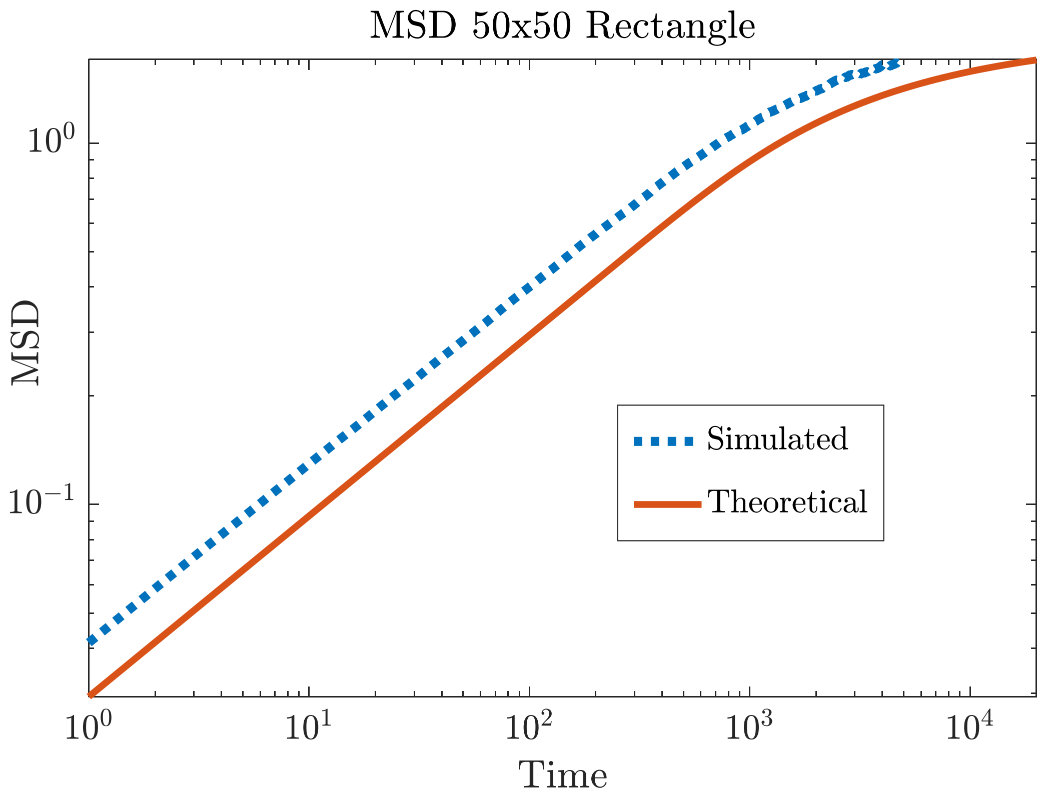
Results

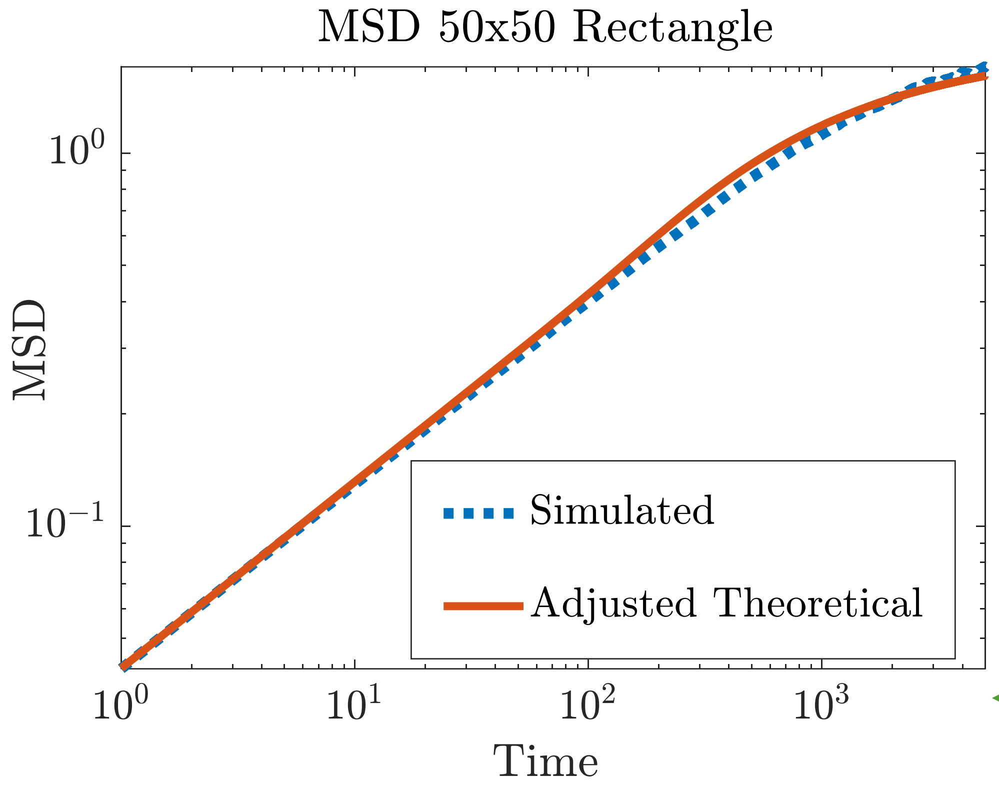
$$\langle (N_c(t+t_0) - N_c(t_0)^2 \rangle = 2N_0 \left[\left(1 - e^{-\frac{W^2}{4Dt}}\right) \sqrt{\frac{4Dt}{\pi W^2}} + 1 - \mathrm{erf}\left(\frac{W}{\sqrt{4Dt}}\right) \right]$$

$$B = \frac{H \times W}{W + H}$$

$$\langle (N_c(t+t_0) - N_c(t_0)^2 \rangle = 2N_0 \left[\left(1 - e^{-\frac{B^2}{8Dt}}\right) \sqrt{\frac{8Dt}{2\pi B^2}} + 1 - \mathrm{erf}\left(\frac{B}{\sqrt{8Dt}}\right) \right]$$

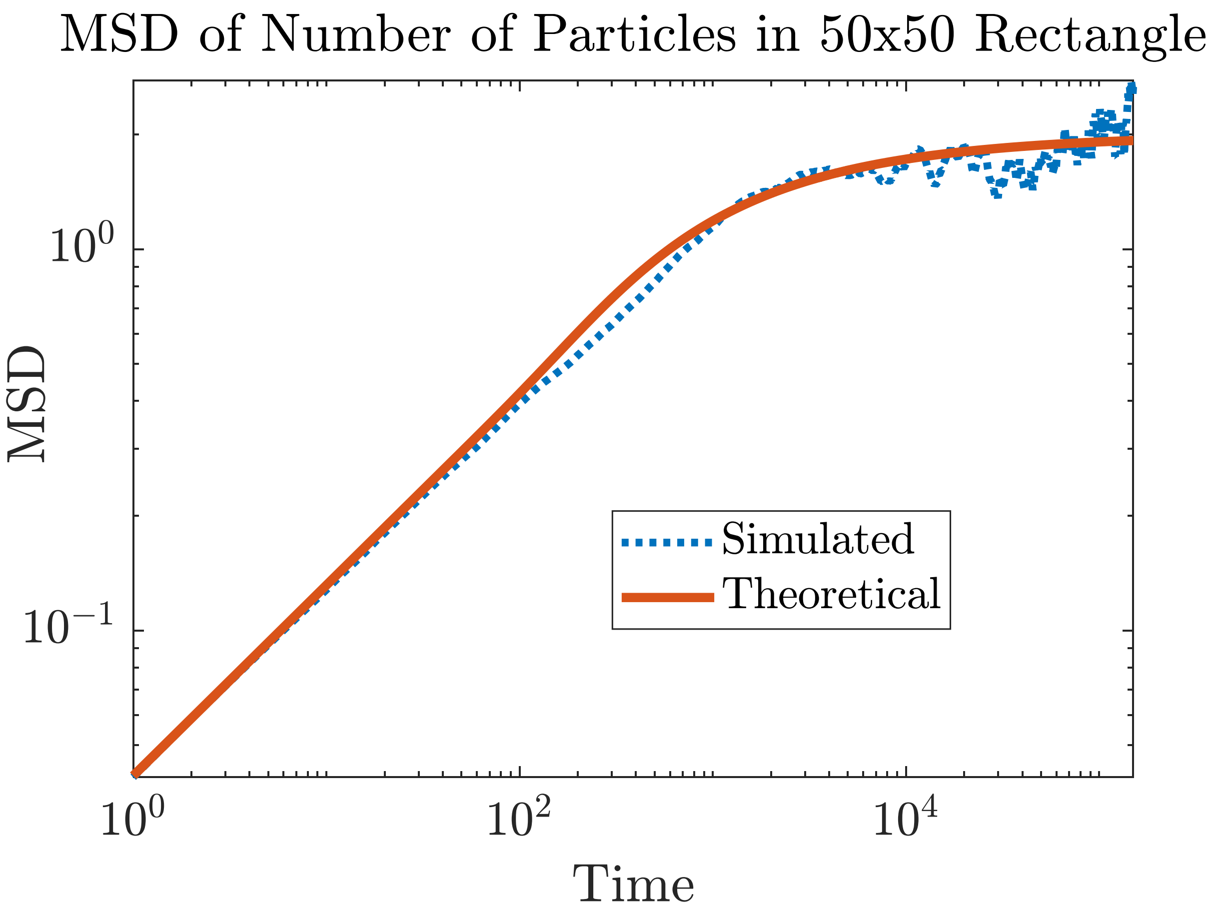
Accounts for added dimension





Only for early times

Future Work



- Look at long times
  - Statistical errors
- When particles have finite size
  - Limited number of particles in the box

Thank You!

Questions?