Electrophoresis of a polyelectrolyte attached to a solid object:

A strong influence of the attachment point

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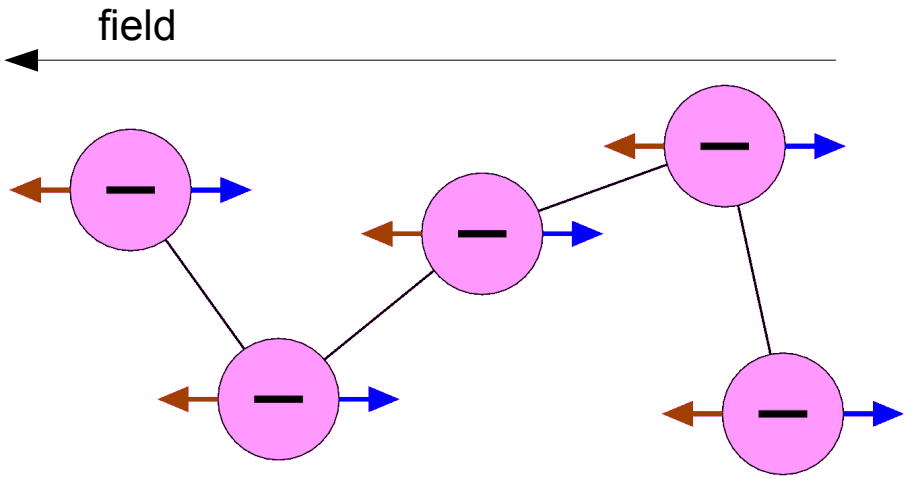
Electrophoresis: motion of charged objects in a fluid in an electric field

When a uniformly charged polymer (e.g., DNA) undergoes electrophoresis, hydrodynamic interactions (HI) between its parts decay rapidly (over ~ Debye length), so different parts interact with the fluid independently (free-draining)



Balance:

friction force electrostatic force

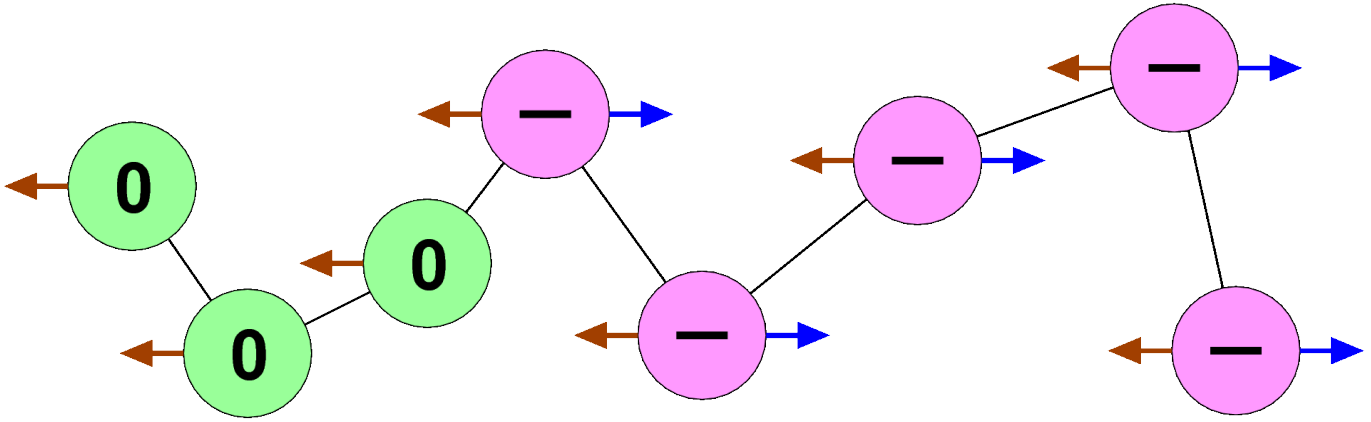
$$\zeta v = QE$$

$$v = \frac{Q}{\zeta} E \qquad \text{Mobility} \quad \mu \equiv \frac{v}{E} = \frac{Q}{\zeta}$$

Both Q and ζ are $\sim N_{DNA}$, so μ is independent of N_{DNA} .

No separation by length in free solution (without a sieving medium).

Attach a neutral polymer to the DNA:



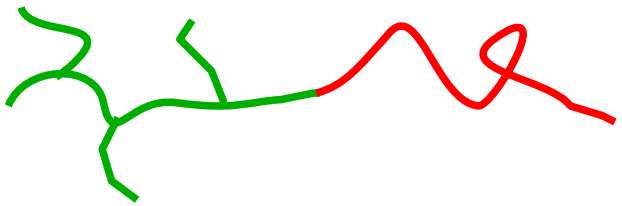
$Q \sim N_{DNA}$. If we naïvely assume free-draining, then $\zeta \sim N_{DNA} + \alpha$.

$$\mu = \frac{Q}{\zeta} \sim \frac{N_{DNA}}{N_{DNA} + \alpha}$$

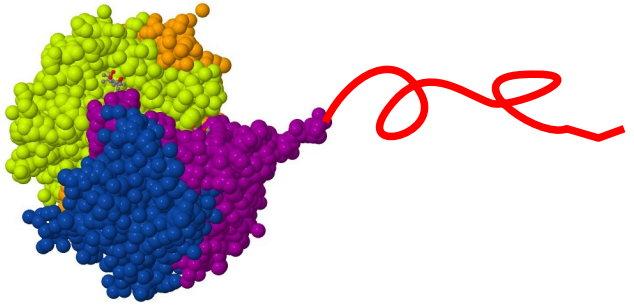
DNA separation becomes possible. End-labeled free-solution electrophoresis (ELFSE).

Mayer *et al.*, Anal. Chem. **66** (1994) 1777; Meagher *et al.*, Electrophoresis **26** (2005) 331

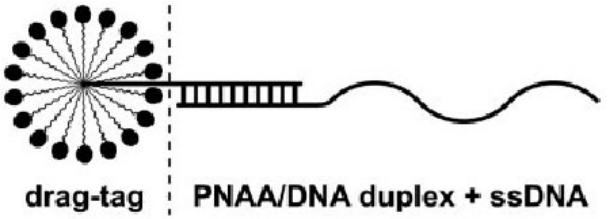
In fact, under the free-draining assumption, it does not matter what the nature of the neutral part is.



Branched polymer



Globular protein



Micelle

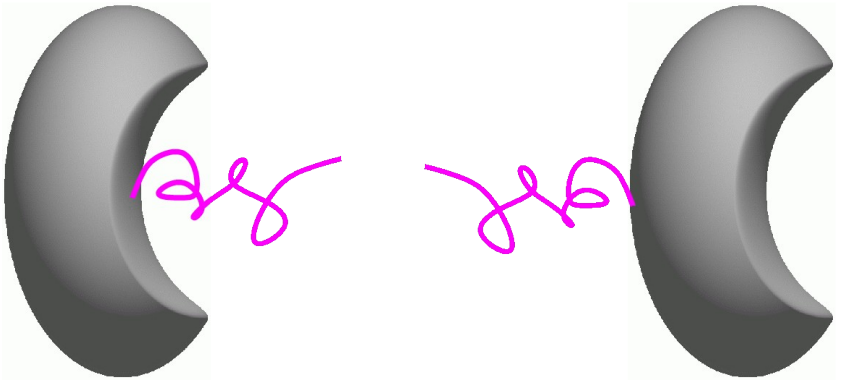
Savard *et al.*, Electrophoresis 29 (2008) 2779.

$$\mu \sim \frac{N_{\mathrm{DNA}}}{N_{\mathrm{DNA}} + \alpha}$$

1. This dependence remains the same regardless of the nature of the neutral part.

2. Constant α is the same for different objects with the same friction coefficient.

3. For a given object, α does not depend on how it is attached.



Free-draining assumption for electrophoresis often assumed reasonably accurate.

Fits to experimental data often look quite good – although sometimes they are not as good as they seem [Chubynsky & Slater, Electrophoresis 35 (2014) 596].

In this talk, an example of a situation where:

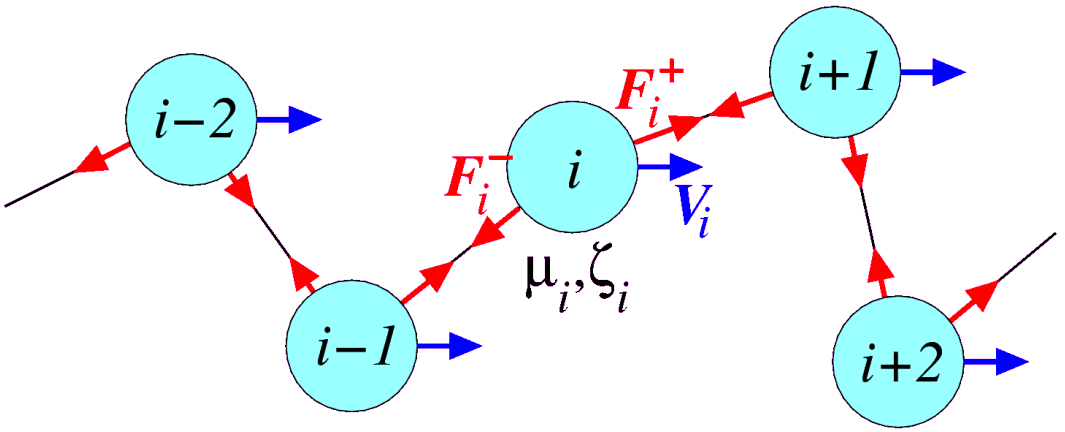
1. The $\mu(N_{DNA})$ dependence is very different (exponential).

2. For different neutral objects with the same friction, the mobility can differ by several orders of magnitude.

3. For a given neutral object, changing the attachment point changes the mobility by several orders of magnitude.

Computational approach (small Debye length limit)

Long *et al.*, J. Phys.: Cond. Mat. 8 (1996) 9471; J. Chem. Phys. 108 (1998) 1234



due to E-force | due to tension | due to HI

$$V^i = \mu_i E + \underbrace{F^i/\zeta_i + \sum_{j\neq i} \hat{H}^{ij} F^j}_{\sum_j \hat{H}^{ij} F^j}$$

$$F^i = F_i^- + F_i^+$$

$$\hat{H}^{ij} = \frac{1}{8\pi\eta r_{ij}}\left(\hat{I} + \frac{r_{ij}\otimes r_{ij}}{r_{ij}^2}\right), \quad i\neq j \qquad \text{(Oseen tensor)} \qquad \hat{H}_{ii} = \frac{1}{\zeta_i}$$

Take the average. Assume $\langle \hat{H}^{ij} F^j\rangle = \langle \hat{H}^{ij}\rangle\langle F^j\rangle$ (Kirkwood-Riseman approx.)

$$\langle \hat{H}^{ij}\rangle = \frac{1}{6\pi\eta}\left\langle \frac{1}{r_{ij}}\right\rangle \hat{I} \quad \text{– scalar}$$

$$\langle V^i\rangle = \mu_i E + \sum_j \langle \hat{H}^{ij}\rangle\langle F^j\rangle \quad \Rightarrow \quad \langle F^i\rangle = \sum_j G^{ij}\left(\langle V^j\rangle - \mu_j E\right), \quad \text{where } G = \langle H\rangle^{-1}$$

Using $\sum_i F^i = 0$ (no external non-electric forces) and $\langle V^i\rangle \equiv V$ (chain moves as a whole),

$$\mu = \frac{V}{E} = \frac{\sum_{i,j} G^{ij}\mu_j}{\sum_{i,j} G^{ij}} = \frac{\sum_j \Gamma_j \mu_j}{\sum_j \Gamma_j}, \quad \text{where} \quad \Gamma_j = \sum_i G^{ij}, \quad G = \langle H\rangle^{-1}$$

$$\mu = \Sigma_j \Psi_j \mu_j, \quad \Psi_i = \frac{\sum_j G^{ij}}{\sum_{i,j} G^{ij}}. \qquad \langle H^{ij} \rangle = \frac{1}{6\pi\eta} \left\langle \frac{1}{r_{ij}} \right\rangle, \quad \langle H^{ii} \rangle = \frac{1}{\zeta_i}.$$

$G = \langle H \rangle^{-1}$. Friction coefficient $\zeta = \Sigma_i \Gamma_i = \Sigma_{i,j} G^{ij}$.

Generate the conformations, calculate H^{ij} for each, average and invert.

Electrostatic analogies

For a rigid object, only orientational averaging, r_{ij} are fixed.

$$\sum_j H^{ij} q_j = \frac{1}{6\pi\eta} \phi_i \;\Rightarrow\; q_i = \frac{1}{6\pi\eta} \sum_j G^{ij} \phi_j.$$

ϕ_j is the potential on the surface of a bead j (assumed spherical).

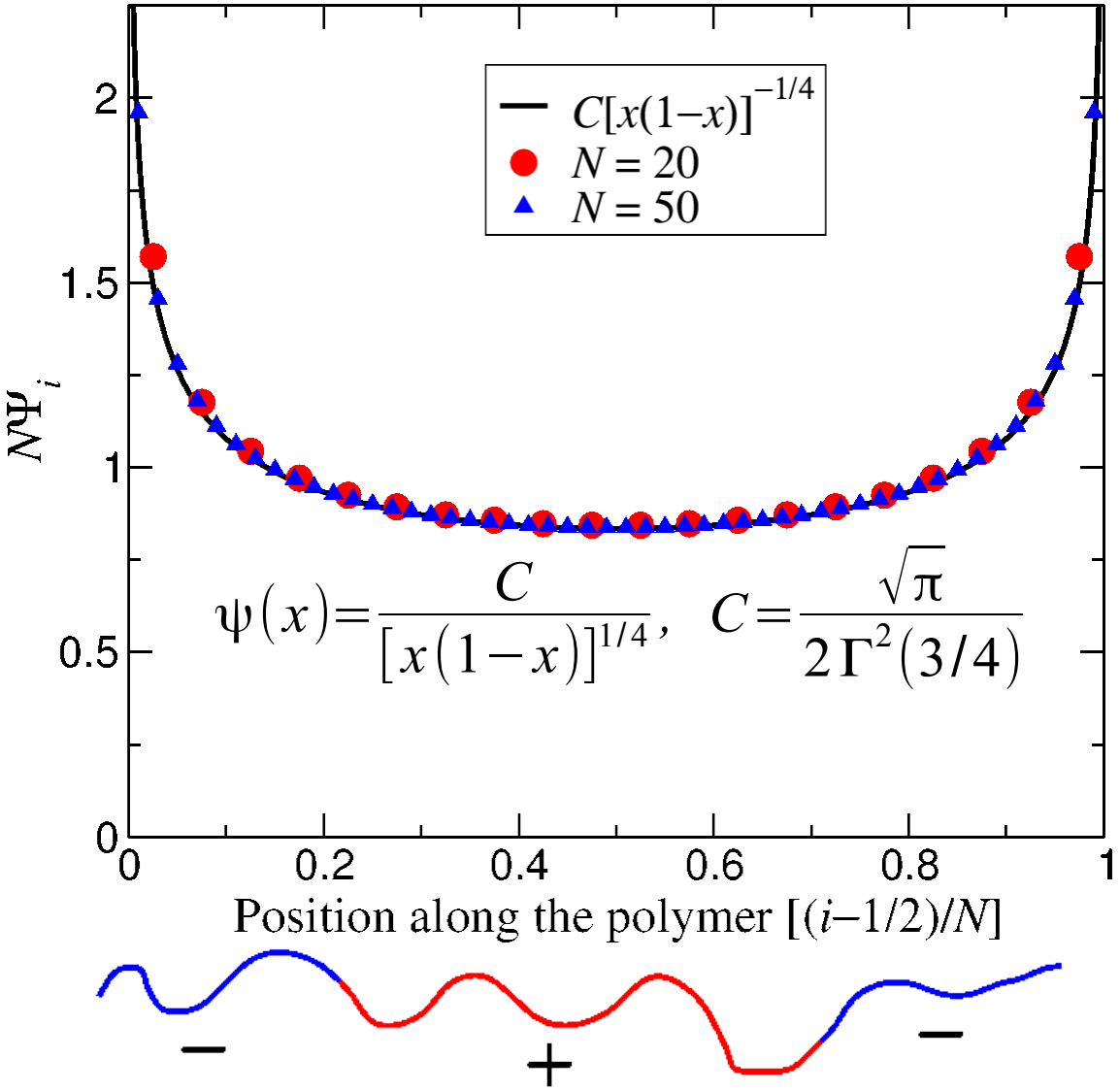
If $\phi_j \equiv 1$, $q_i = \frac{1}{6\pi\eta} \sum_j G^{ij}$. $\qquad \Psi_i = \frac{q_i}{\Sigma_j q_j}$

1. The weight of a bead is equal to the fraction of the total charge at that bead when the whole system is held at unit potential.

2. Suppose one bead is held at unit potential and the rest are at 0. The weight of the bead is proportional to the total charge. Screening problem. The better the charge of a bead would be screened by the rest, the lower its weight.

Gaussian chain (fully flexible, no excluded volume)

Monomer numbers are $i = 1, 2, \ldots, N$ along the chain.



Ends contribute more – moves as "-" charged

Long *et al.*, JCP 108 (1998) 1234

Chubynsky & Slater, Electrophoresis 35 (2014) 596

Ends contribute more.

Qualitatively, expected: think charged metal plates, where edges have a higher charge density.

Long *et al.*, JCP 108 (1998) 1234

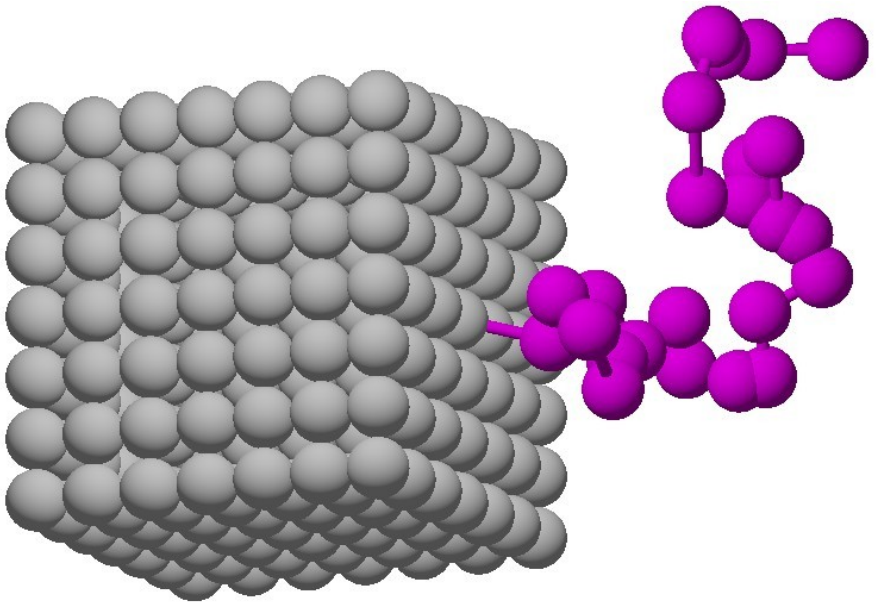
Hickey et al., PRL 105 (2010) 148301

Hickey & Holm, JCP 138 (2013) 194905

A chain attached to a solid object

A nanoparticle, a globular protein, or a micelle.

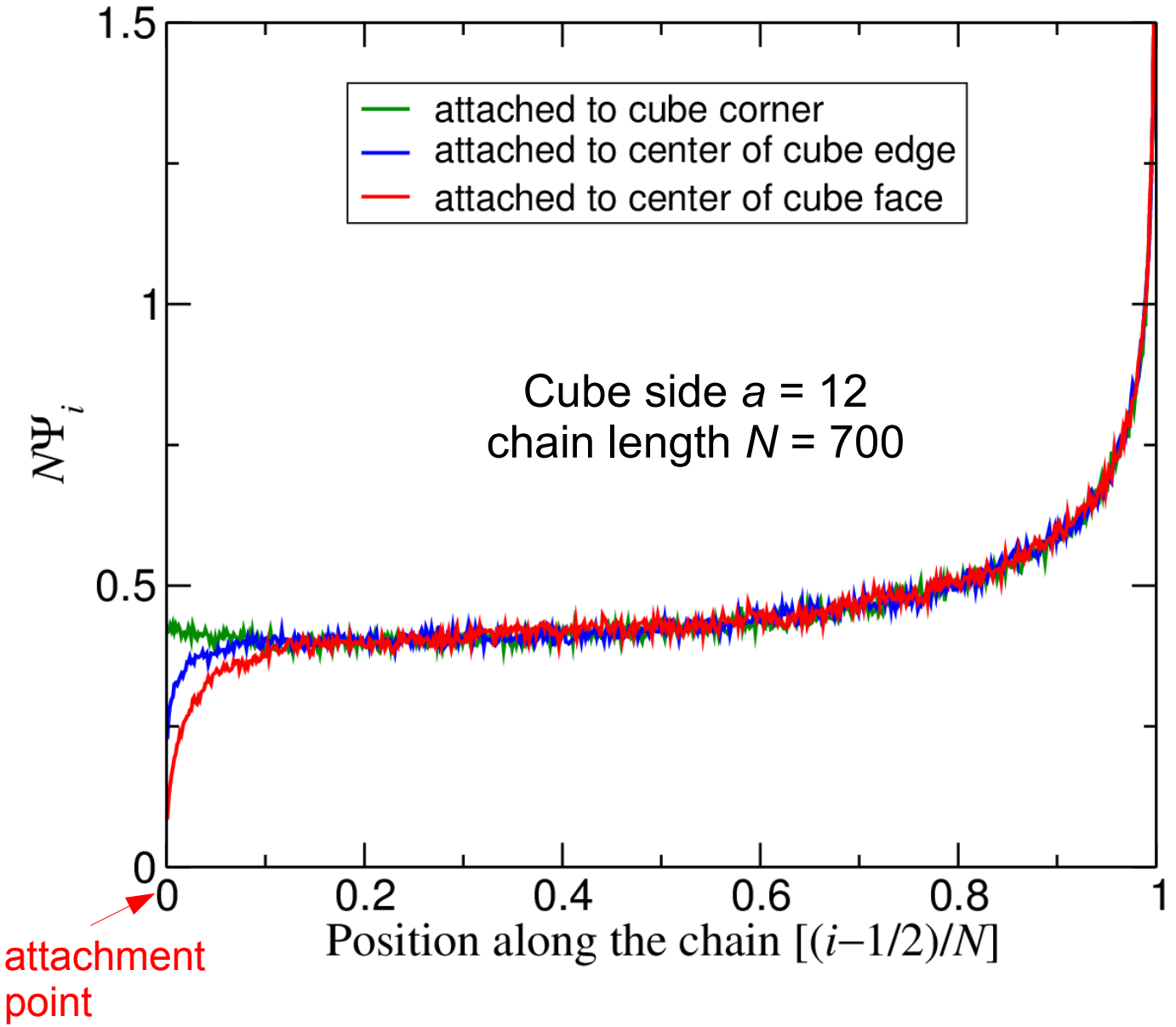
A **cube** is a convenient model, both computationally and to test the attachment point dependence.

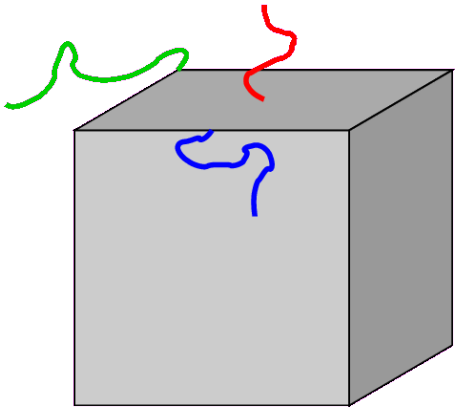


Hollow inside (think hollow vs. solid metal sphere). For a cube with side a, $(a+1)\times(a+1)$ beads per face. RMS bond length of the polymer is 1.

Charges closer to the cube are screened better/the potential deficit is smaller $\Rightarrow$ the weights should decrease towards the cube. The effect depends on the attachment point.

Different attachment points. Weights.





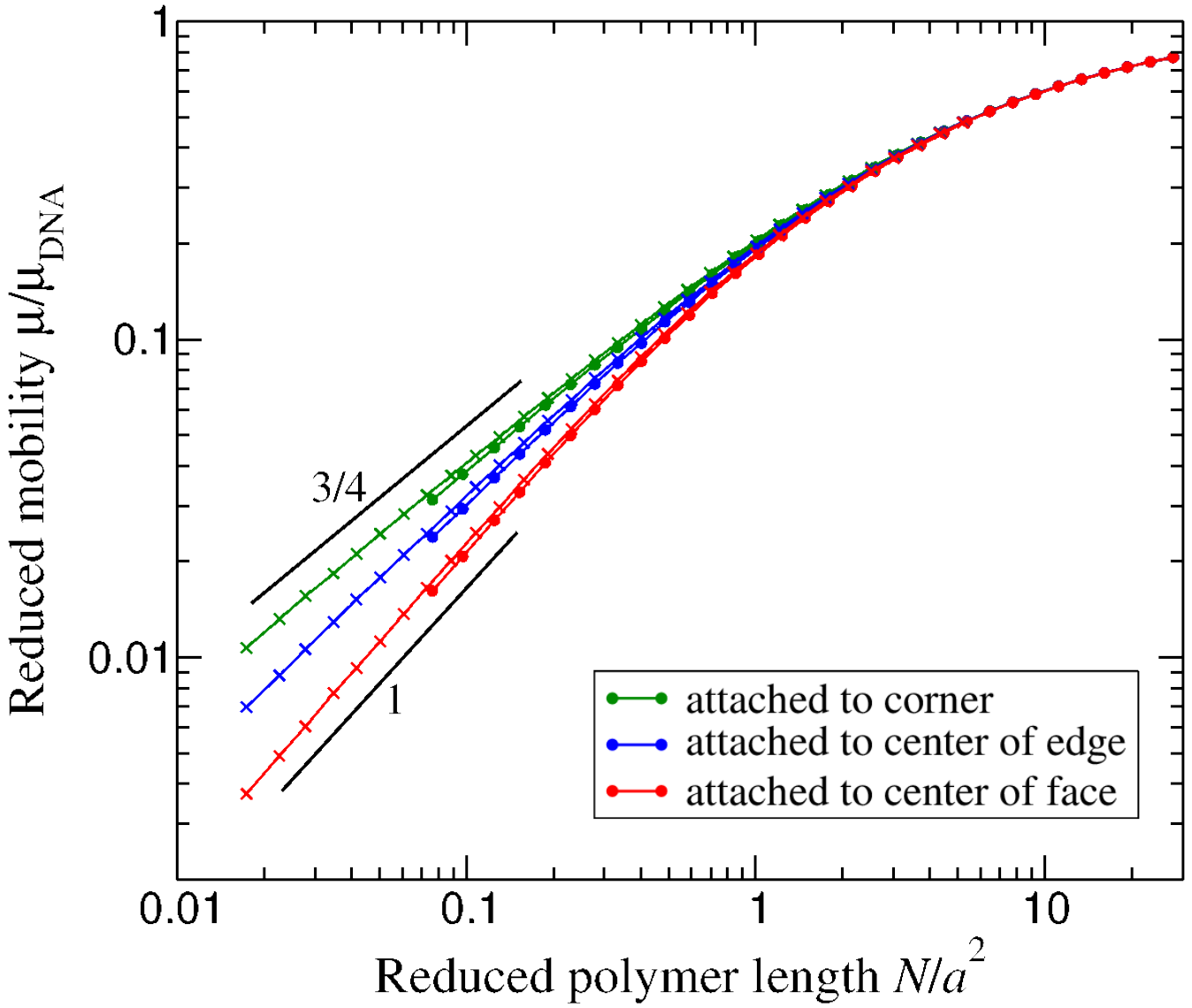
Face: $\Psi_i \propto i^{1/2}$

Edge: $\Psi_i \propto i^{1/6}$

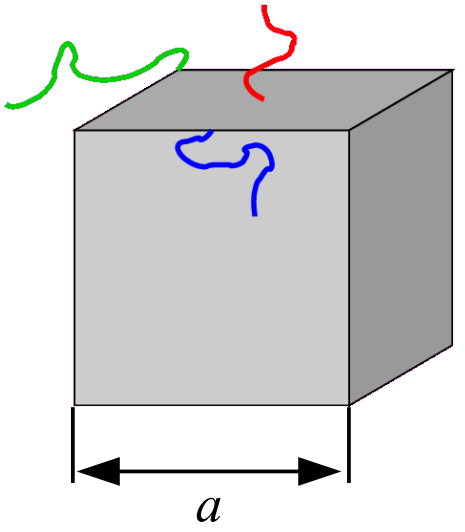
Corner: $\Psi_i \propto i^{0}$

Charges near a corner or an edge are screened less efficiently.

Different attachment points. Mobilities.



● : $a=12$ ×: $a=24$



$$N/a^2 \simeq (R_g/a)^2$$

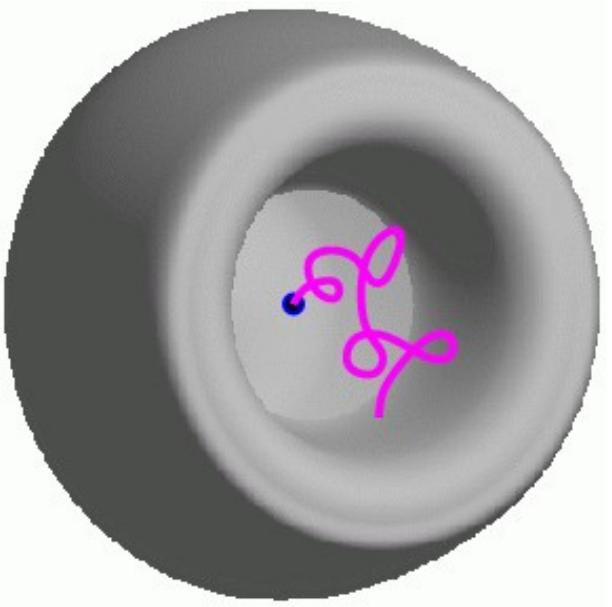
Recall that in simple theory

$$\frac{\mu}{\mu_{DNA}} \sim \frac{N}{N+\alpha} \propto N$$

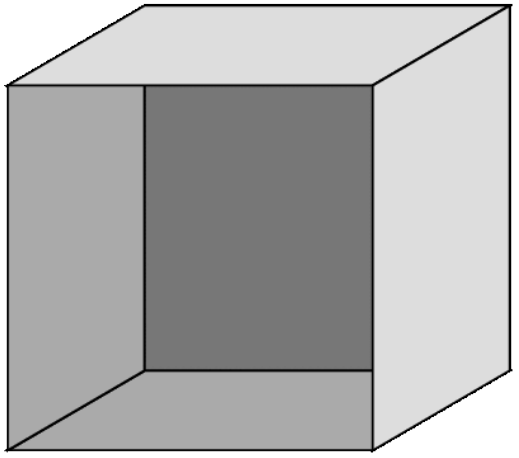
Different exponents at small N

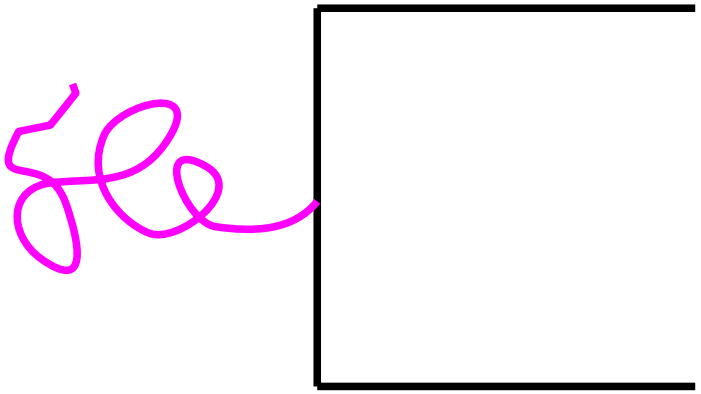
How can we make this attachment point dependence effect more dramatic?

For an object with a cavity, screening inside the cavity is very effective.

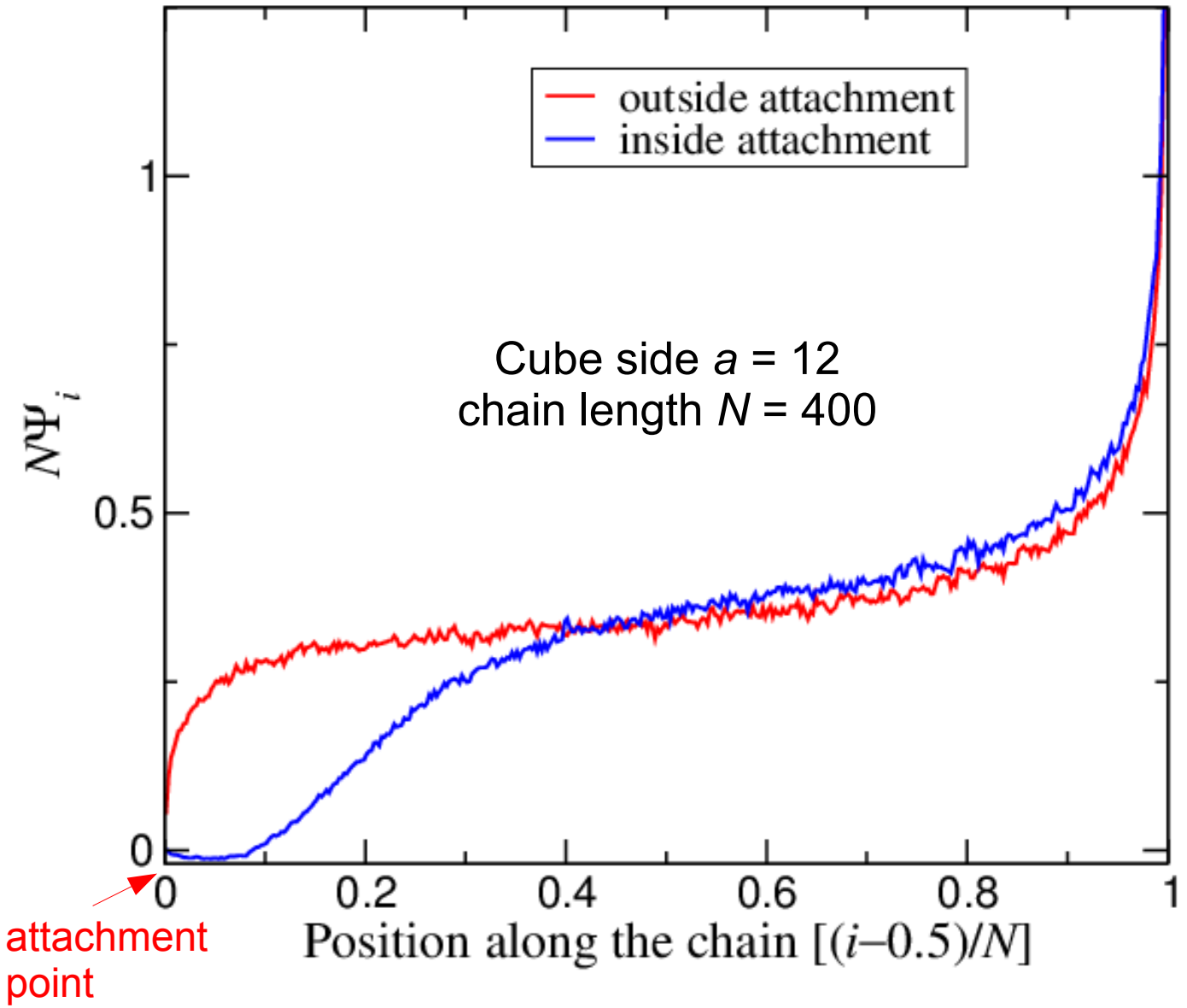


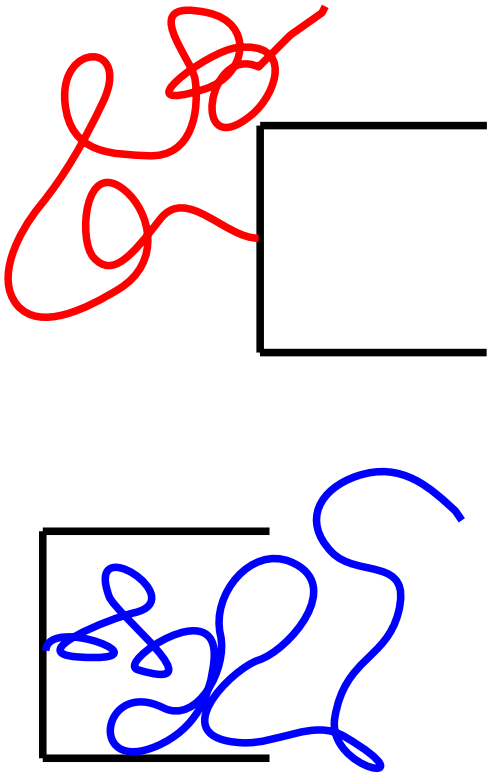
Model this by considering a cube shell (as before), but removing one face of the cube. Attach the polymer to the face opposite to the removed one. Inside vs. outside attachment.





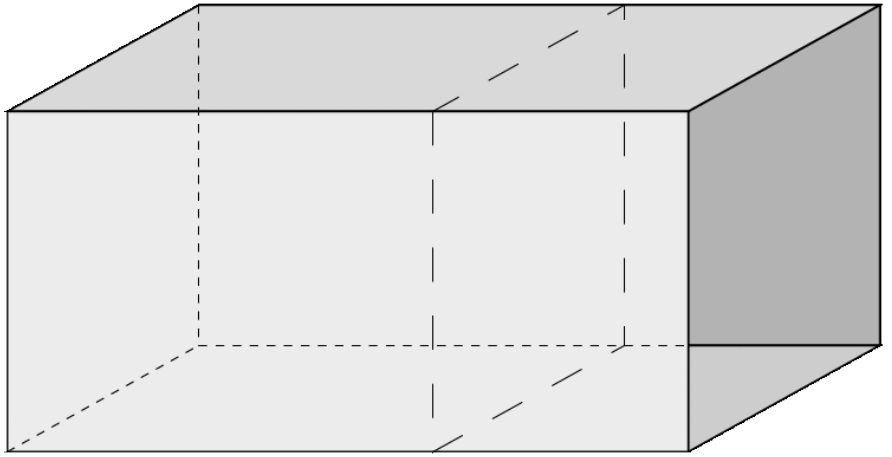
Inside vs. outside attachment. Weights.



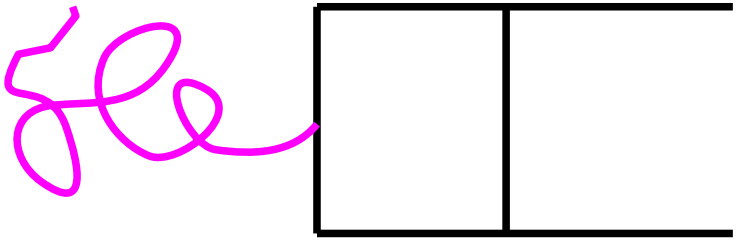


Weights of the part of the chain inside the cavity are very low.

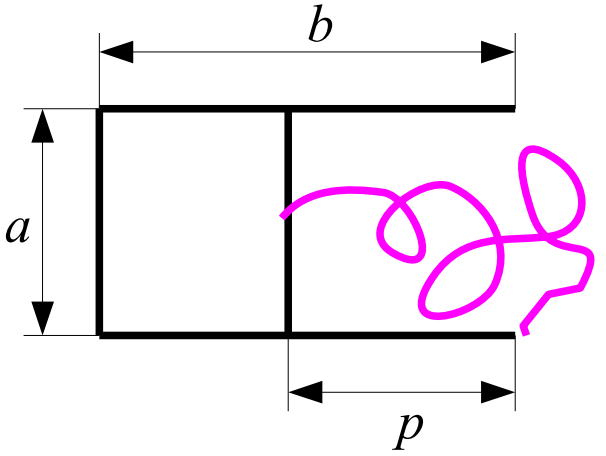
To study the influence of cavity depth, consider a parallelepiped cavity with a plate inside that can change its position. The friction coefficient is independent of the plate position to within 1%.



In cross-section:

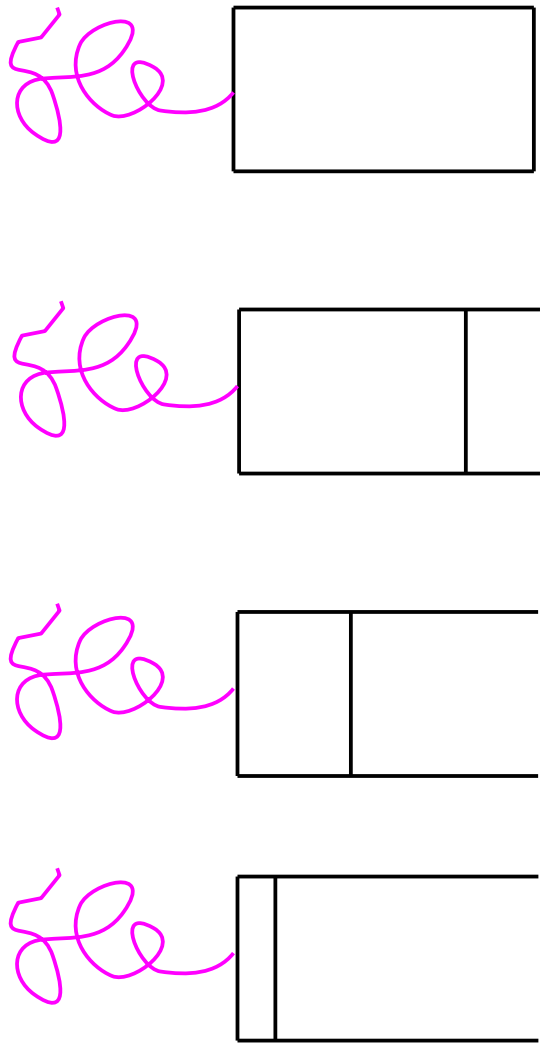


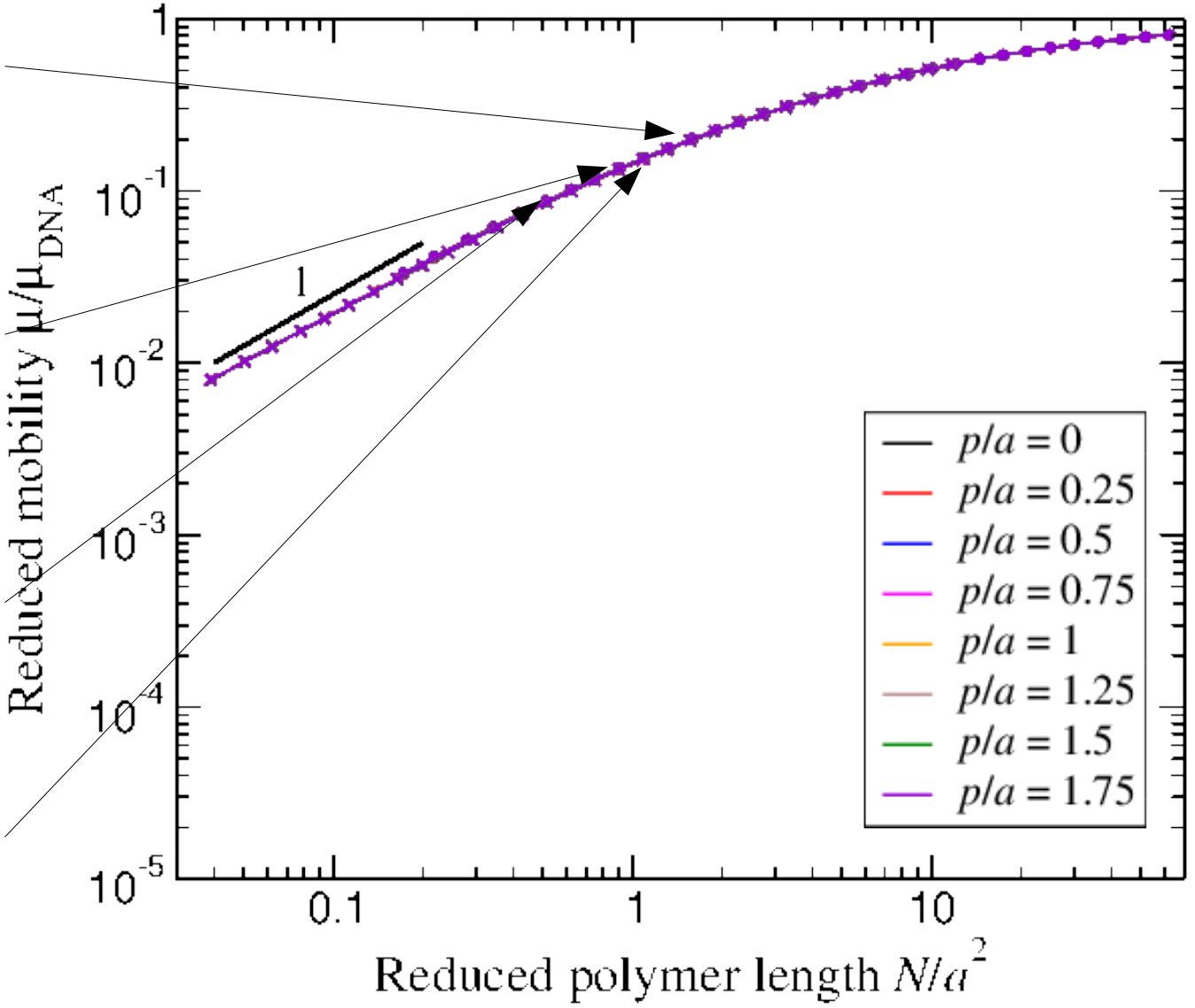
Outside attachment



Inside attachment

Mobilities (**outside** attachment)

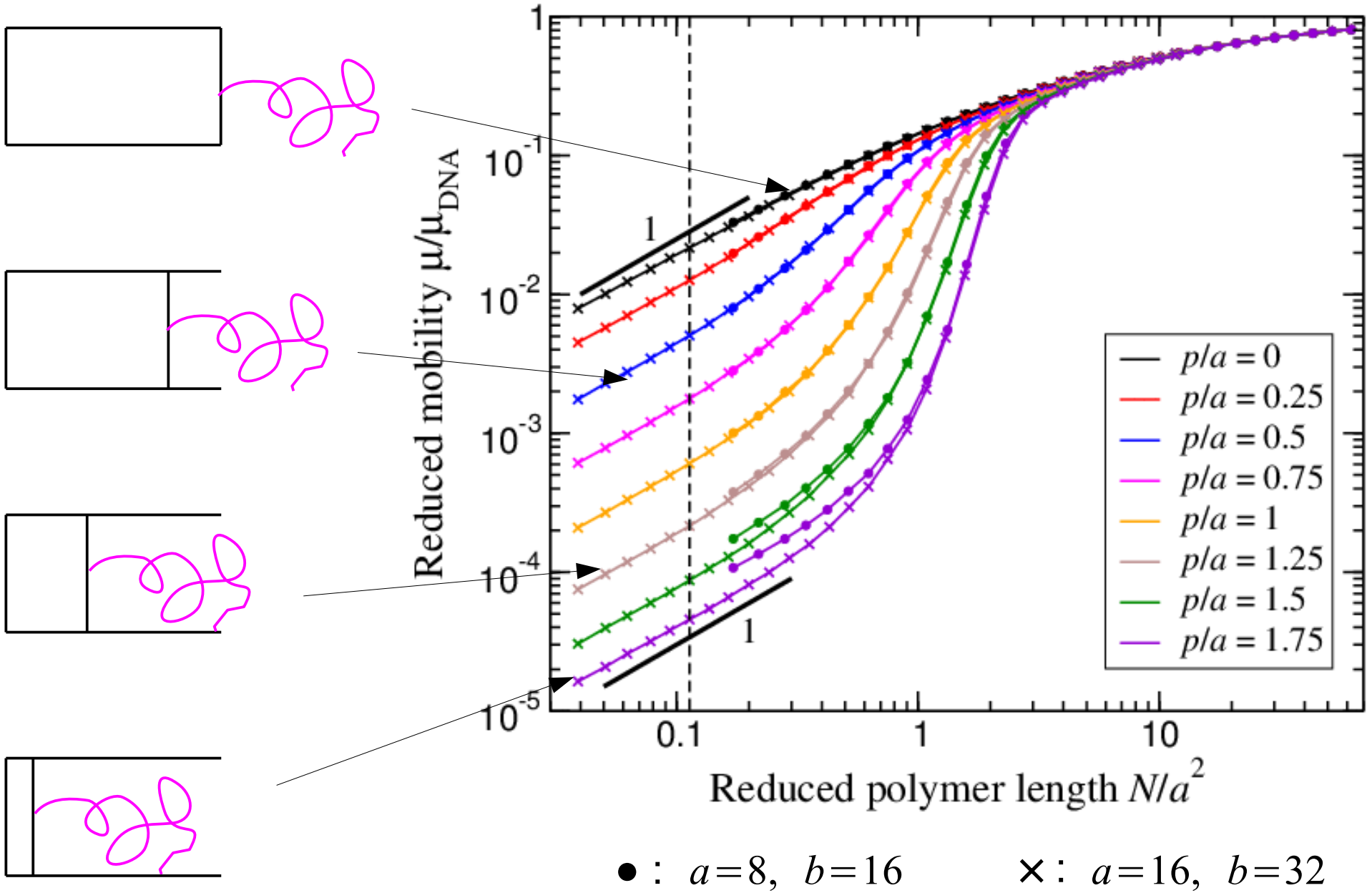




● : $a=8,\ b=16$ ×: $a=16,\ b=32$

No plate position dependence

Mobilities (**inside** attachment)



● : $a=8,\ b=16$ ×: $a=16,\ b=32$

Very strong plate position and N dependence

We have found that when a charged polymer is attached to a neutral object with a cavity, the mobility of the resulting complex depends significantly on whether the attachment point is inside the cavity, provided that the polymer fits inside it.

The effect is significant even for fairly shallow cavities and depends strongly (exponentially) on the cavity depth.

Very strong polymer size dependence of the mobility when its radius of gyration is comparable to the cavity size $\Rightarrow$ potential separation applications.

Need to go beyond approximations we have used (particularly, pre-averaging). Very preliminary results show additional interesting effects.

$$\mu = \Sigma_j \Psi_j \mu_j, \qquad \Psi_i = \frac{\sum_j G^{ij}}{\sum_{i,j} G^{ij}}. \qquad \Sigma_i \Psi_i = 1.$$

$$G = \langle H \rangle^{-1}. \qquad G^{ij} = G^{ji}$$

$$\langle H^{ij} \rangle = \frac{1}{6\pi\eta} \left\langle \frac{1}{r_{ij}} \right\rangle, \quad \langle H^{ii} \rangle = \frac{1}{\zeta_i}.$$

For a rigid object, only orientational averaging, r_{ij} are fixed.

Electrostatic analogies

$$\frac{1}{6\pi\eta}\phi_i = \Sigma_j H^{ij} q_j \;\Rightarrow\; q_i = \frac{1}{6\pi\eta}\Sigma_j G^{ij}\phi_j.$$

ϕ_j is the potential on the surface of a bead j (assumed spherical).

If $\phi_j \equiv 1$, $q_i = \frac{1}{6\pi\eta}\Sigma_j G^{ij} = \frac{1}{6\pi\eta}\Gamma_i.$ $\qquad \Psi_i = \frac{q_i}{\Sigma_j q_j}$

1. The weight of a bead is equal to the fraction of the total charge at that bead when the whole system is held at unit potential.

Remove the charge of bead i. The potentials of nearly all other beads remain ≈1. Denote ϕ'_i the new potential of bead i. The charge q_i needed to restore the potential to 1 is $\propto 1 - \phi'_i$ (potential deficit).

2. The weight of a bead is approximately proportional to the potential deficit at that bead's location when the rest of the beads are held at potential 1.

$$\mu=\Sigma_j \Psi_j \mu_j, \qquad \Psi_i=\frac{\sum_j G^{ij}}{\sum_{i,j} G^{ij}}. \qquad \Sigma_i \Psi_i=1.$$

$$G=\langle H\rangle^{-1}. \qquad G^{ij}=G^{ji}$$

$$\langle H^{ij}\rangle=\frac{1}{6\pi\eta}\left\langle\frac{1}{r_{ij}}\right\rangle, \quad \langle H^{ii}\rangle=\frac{1}{\zeta_i}.$$

Electrostatic analogies (continued)

$$q_i=\frac{1}{6\pi\eta}\sum_j G^{ij}\phi_j. \quad \text{Choose} \quad \phi_j=\delta_{jk}. \quad q_i=\frac{1}{6\pi\eta}G^{ik} \Rightarrow Q\equiv\Sigma_i q_i=\frac{1}{6\pi\eta}\Sigma_i G^{ik}\propto\Psi_k .$$

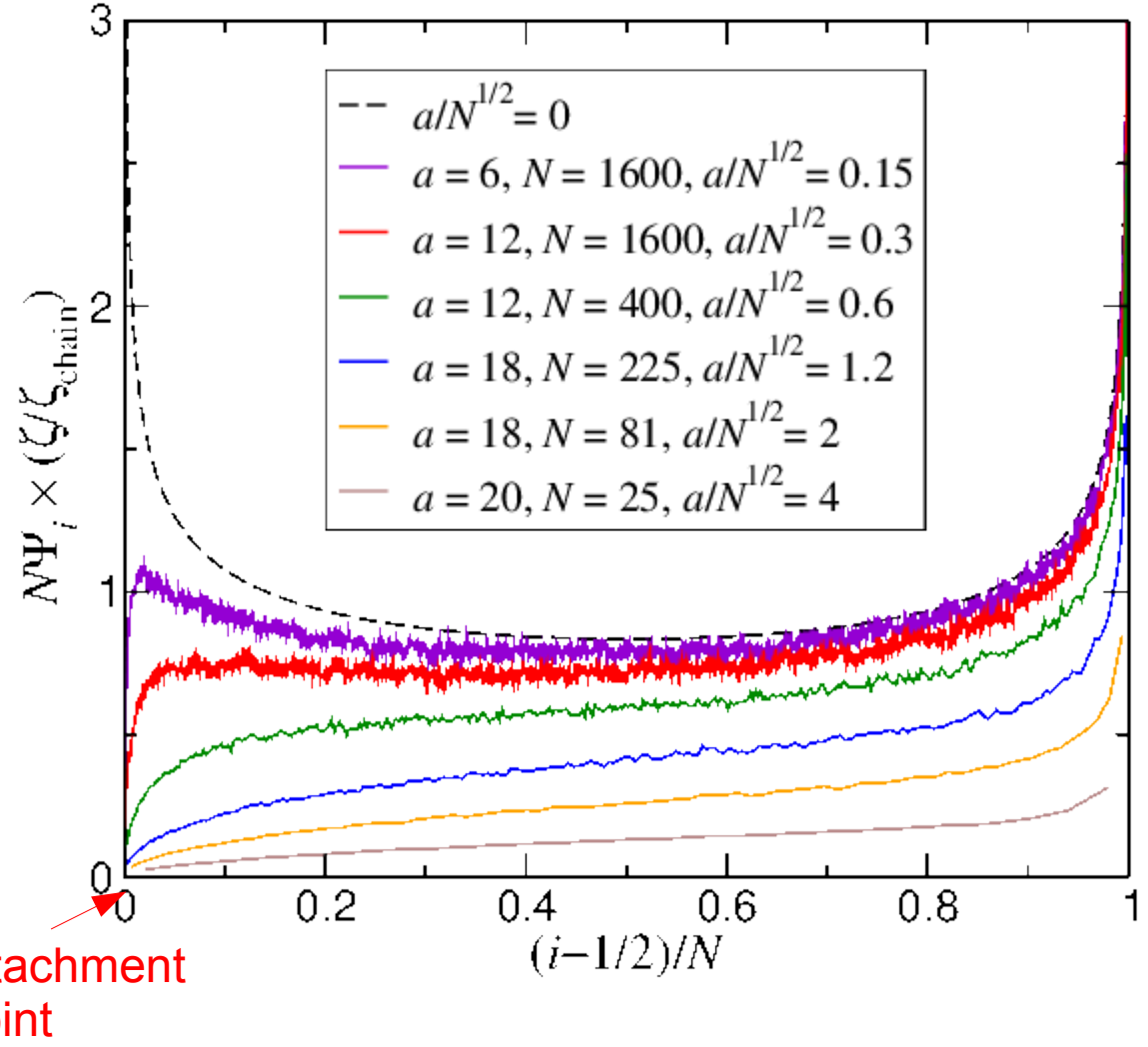
3. The weight of a bead is proportional to the total charge in the case when that bead is held at potential 1 and the rest are held at 0.

Screening problem: the more the charge of a bead is screened by the rest, the less its weight.

These analogies allow easy qualitative analysis of different situations.
Quantitative calculations are done by computing the HI matrix H^{ij} and inverting it.

Chain weights

Plot $\Psi_i \times \frac{\zeta}{\zeta_{\text{chain}}}$. If there were no HI between the chain and the cube, would give isolated chain weights.



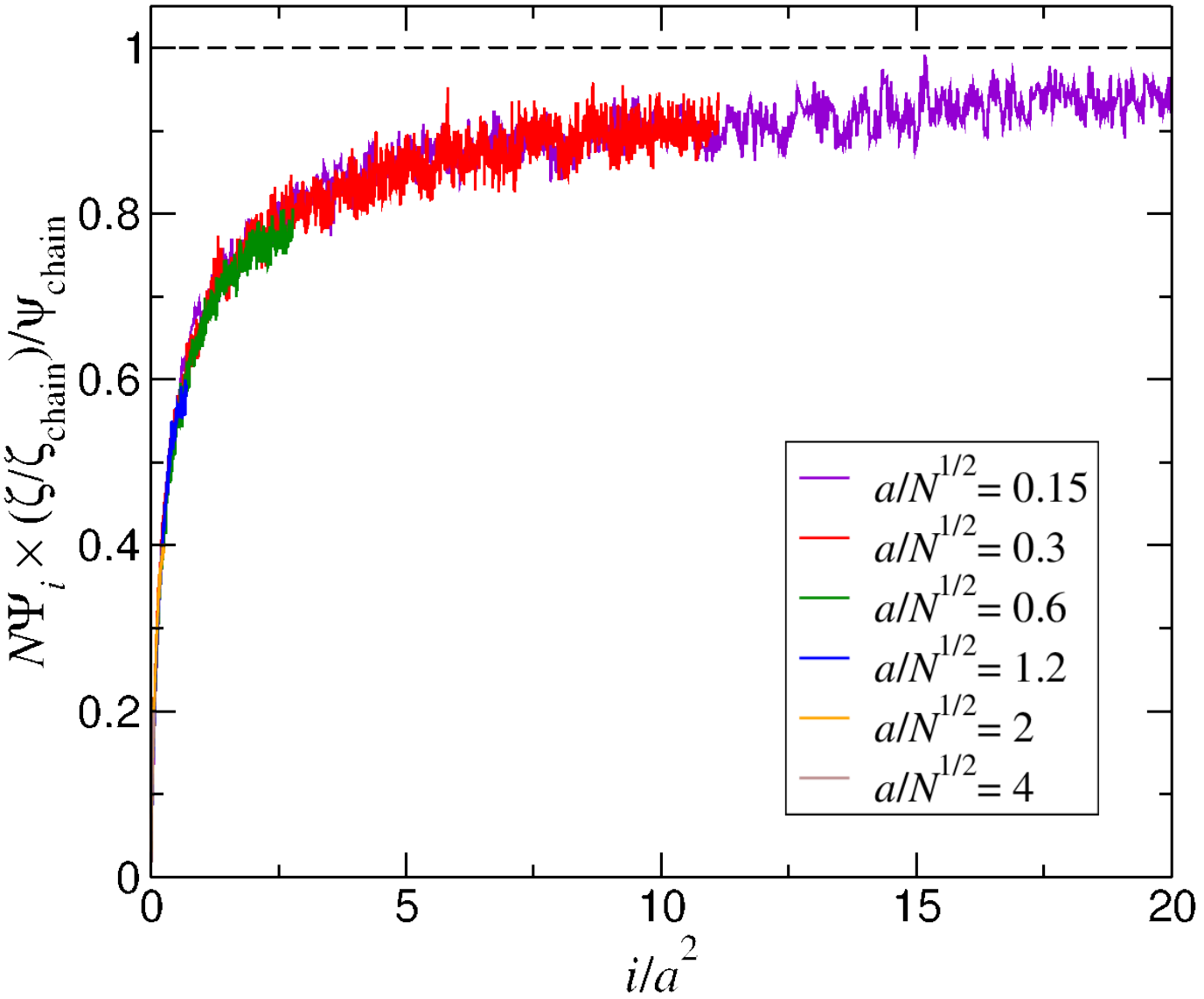
The part of the chain near the attachment point (at zero) matters less.

Chain weights

To show explicitly the influence of the cube, divide by the isolated chain weight

$$\psi_{\text{chain}}(x) = C[x(1-x)]^{-1/4}, \quad x = (i-1/2)/N.$$

The x axis is ~ square of the ratio of the distance from the cube to its size.



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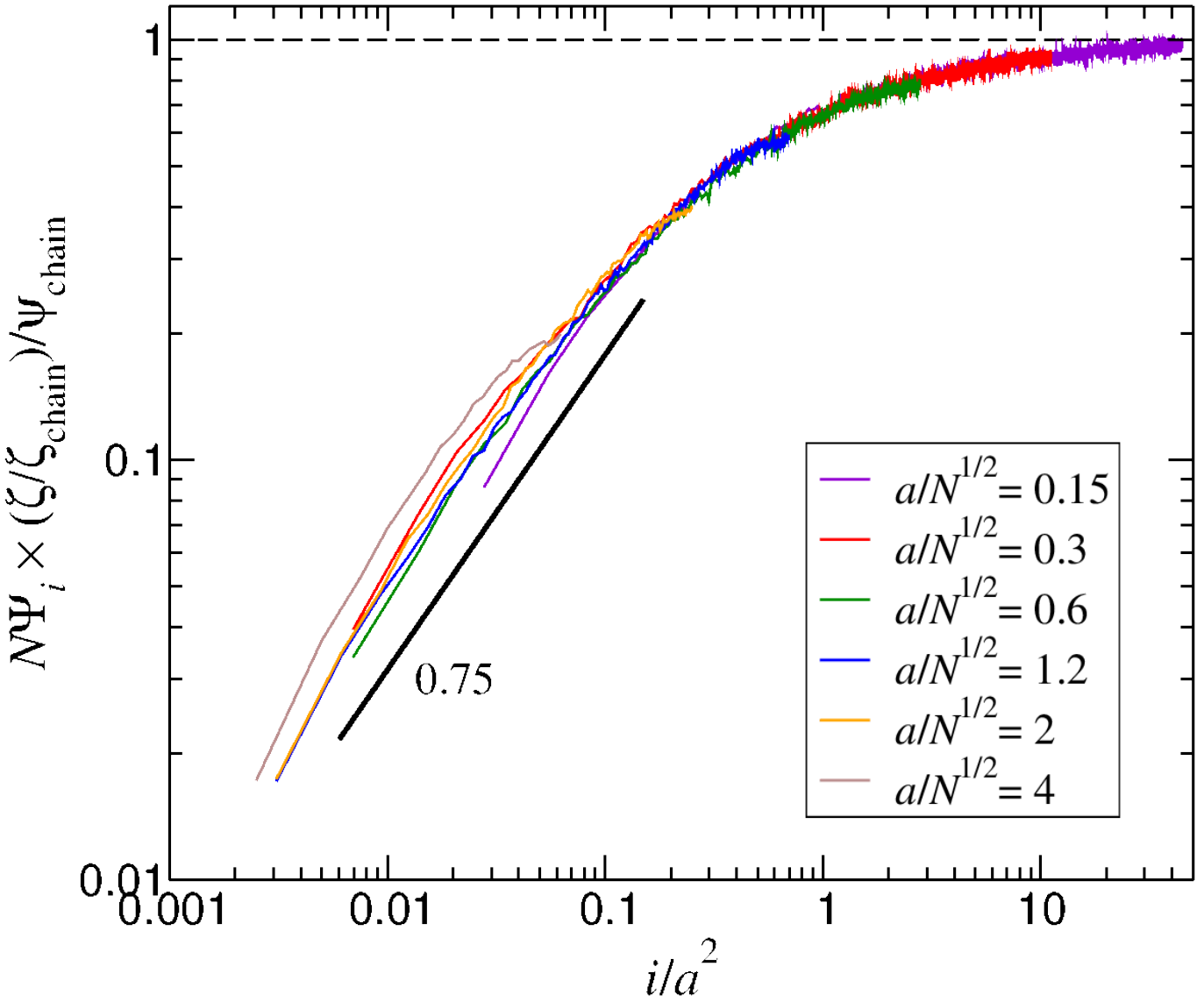


For small N/a^2

$$\Psi_i \propto i^{0.75} \zeta_{\text{chain}} \psi_{\text{chain}} / N$$

$$\propto i^{0.75} \psi_{\text{chain}} N^{-0.5}$$

$$\mu = \mu_{\text{DNA}} \sum_{i=1}^{N} \Psi_i \propto N^{1.25}$$

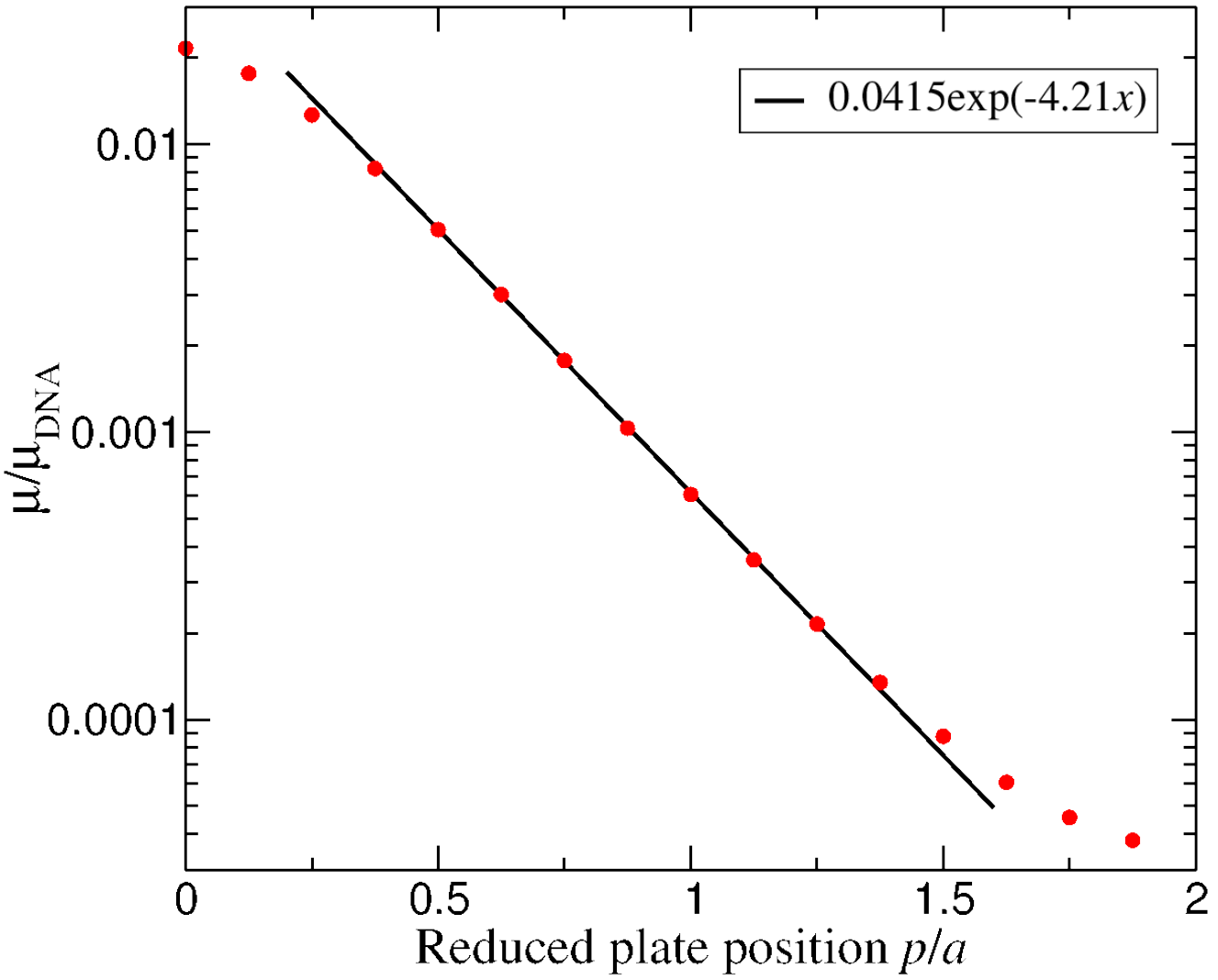
When the neutral object is a flexible linear chain,

$$\mu \propto N^{0.75}$$

For small i/N, N/a^2

$$\Psi_i \propto i^{0.5}$$

Plate position dependence ($N/a^2 = 0.113$)



Exponential.dependence. Mobility decrease by a factor of 35 when depth = width.

4.21 is close to $\pi\sqrt{2}=4.44$ expected from the solution of the Laplace equation for a semi-infinite channel.

If the HI are neglected, H^{ij} is diagonal. If all ζ_i are the same,

$$H^{ij} = H\,\delta_{ij}, \quad G^{ij} = (1/H)\,\delta_{ij}, \quad \Psi_i = \text{const} = 1/N \ .$$

For the case of DNA+(neutral object), $N = N_{DNA} + \alpha$.

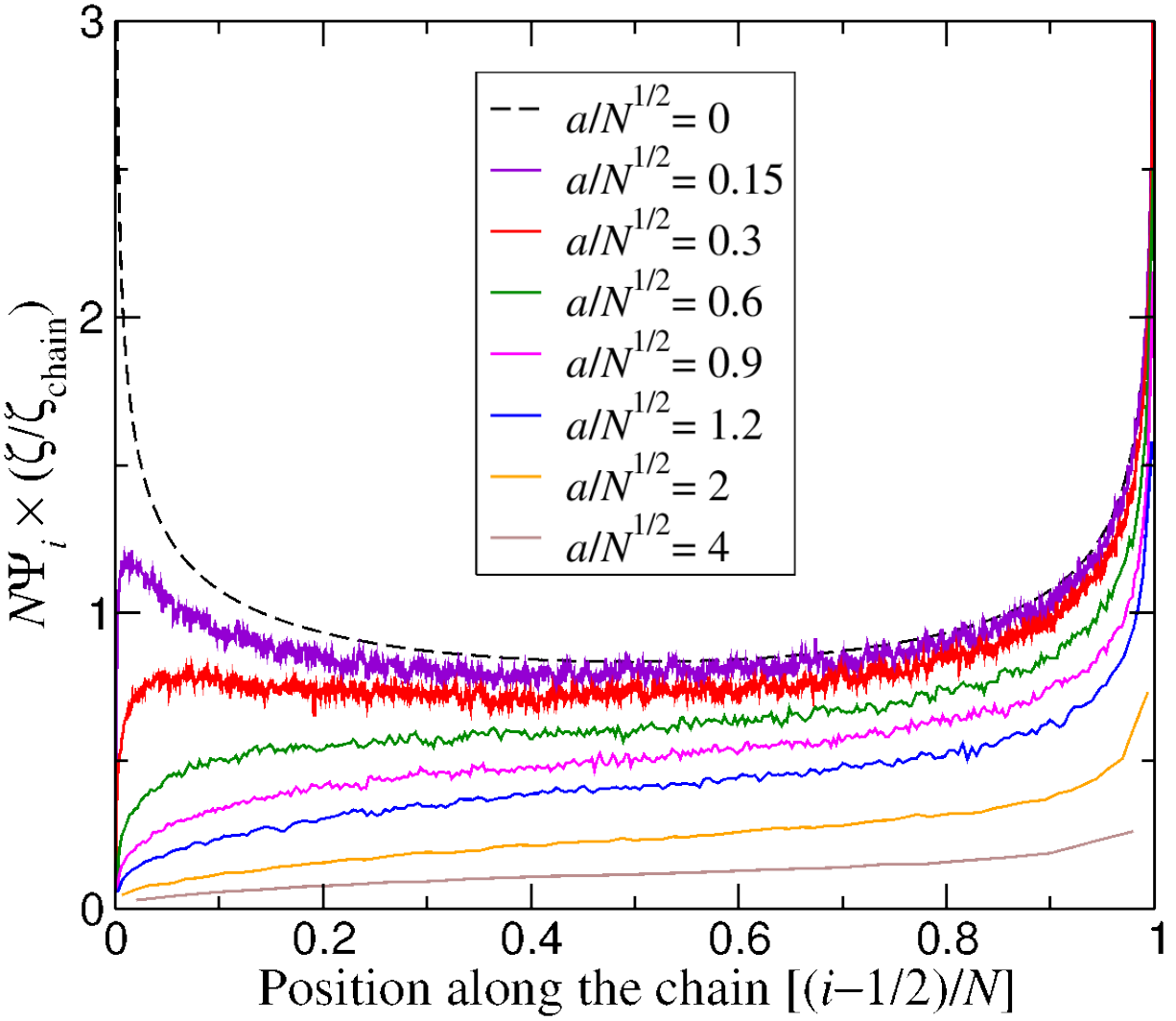
$$\mu = \frac{1}{N_{DNA}+\alpha}\left(N_{DNA}\mu_{DNA} + \alpha \times 0\right) = \frac{N_{DNA}}{N_{DNA}+\alpha}\mu_{DNA}.$$

Can still be done when the system includes solid objects and not just linear chains, by constructing these objects out of beads.

2. Suppose one bead is uncharged and the rest are still at unit potential. The weight of that bead is approximately proportional to the **potential deficit** at its location.

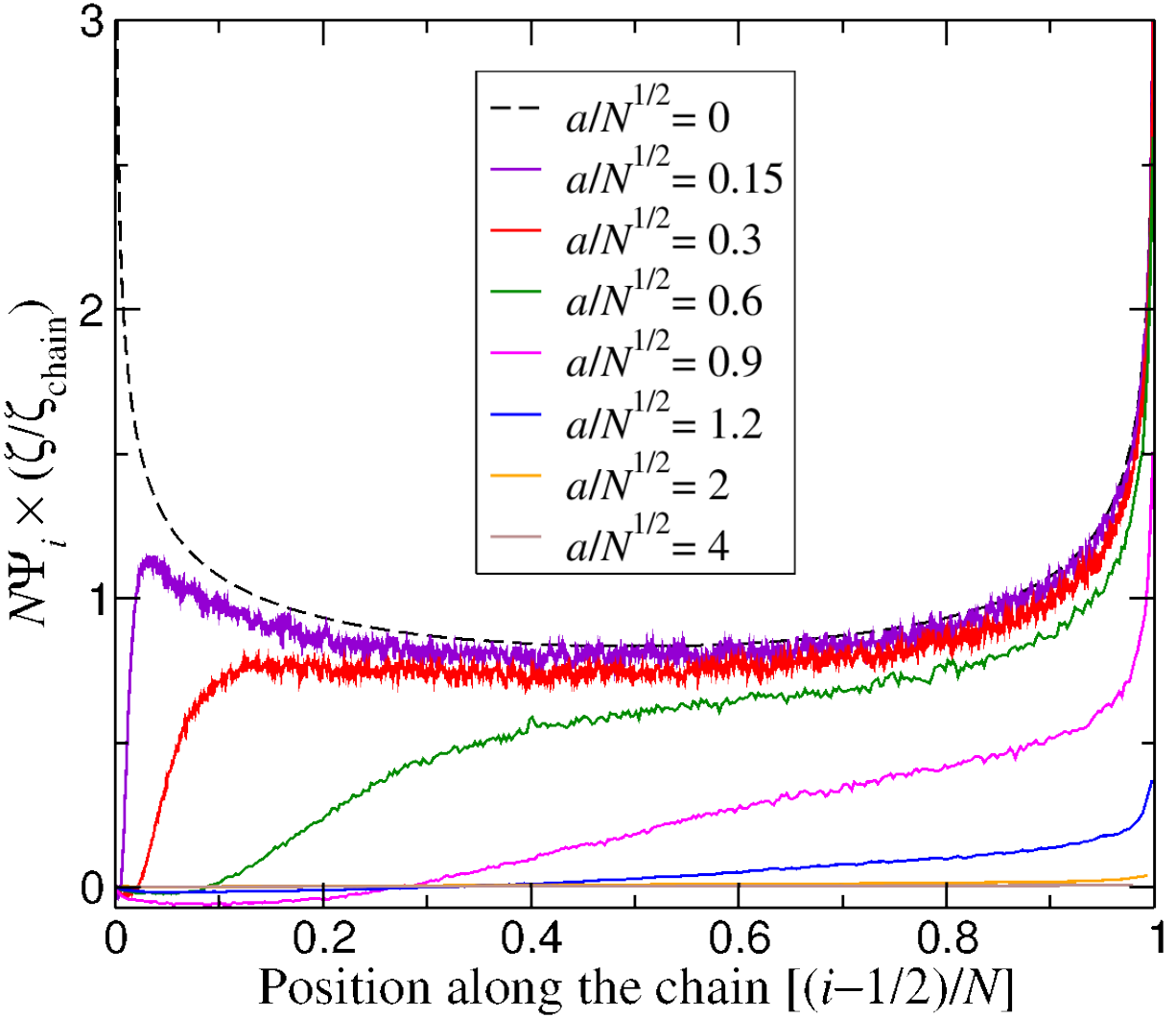
Weights (**outside** attachment)

Plot $\Psi_i \times \frac{\zeta}{\zeta_{\text{chain}}}$. If there were no HI between the chain and the cube, would give isolated chain weights. Nearly identical to the closed cube.

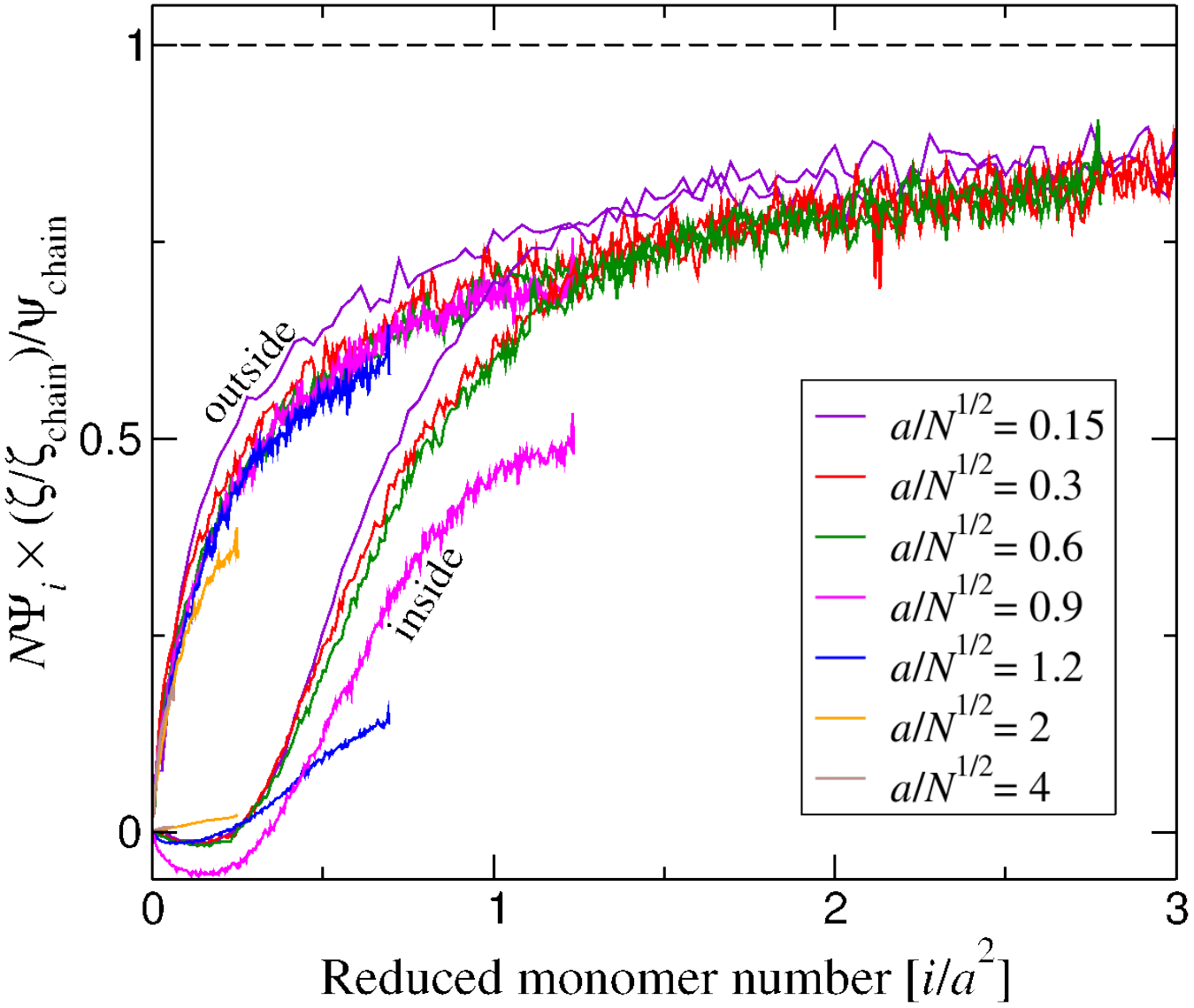


Weights (**inside** attachment)

For $a/N^{1/2} \lesssim 1$, a region where the weights are very low (corresponds to the part of the chain inside the cavity). For $a/N^{1/2} \gtrsim 1$, the entire chain is inside and the weights are low everywhere. Small negative weights probably an artifact.



Weights divided by isolated chain weights



For inside attachment, the part of the chain inside the cavity has much smaller weights.