Understanding structure of polyelectrolytes through simulation and single molecule force measurements

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Theory of *Flexible* Chain Pull

Scaling theory

$R \sim N^{\nu}$ end-to-end distance

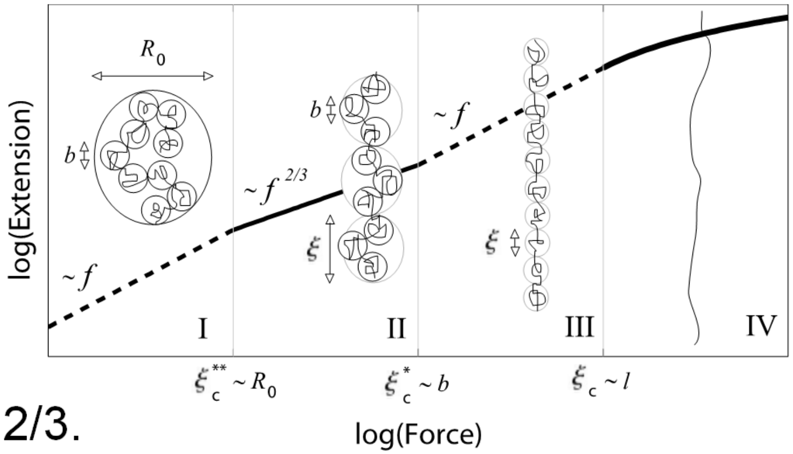
$\xi_t \sim b g^{\nu}$ tension blob size

$f \sim kT / \xi_t$

$R \sim \xi_t N / g$ extension under tension

$R \sim f^{\gamma} \quad \gamma = 1/\nu - 1$

Chain of tension blobs stretched, while chain within tension blob is unstretched.



For a good solvent, neutral chain ν = 3/5 and γ = 2/3.

For ideal chain, ν = 1/2 and γ = 1.

For ssDNA with N = 5000 and 100 mM NaCl,

Debye length = 1 nm $\ll$ L=aN $\Rightarrow$ neutral scaling at large lengths.

But have a distinct ν > 3/5 at short length scales.

Electrostatic blob length is very short 2-3a.

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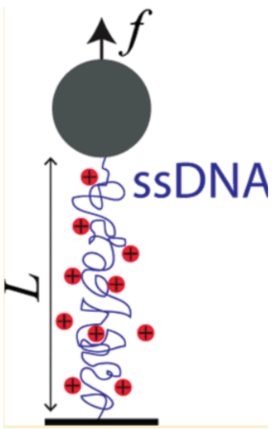
ssDNA system



single stranded

no base-pairing ⇒

flexible, stong polyelectrolyte

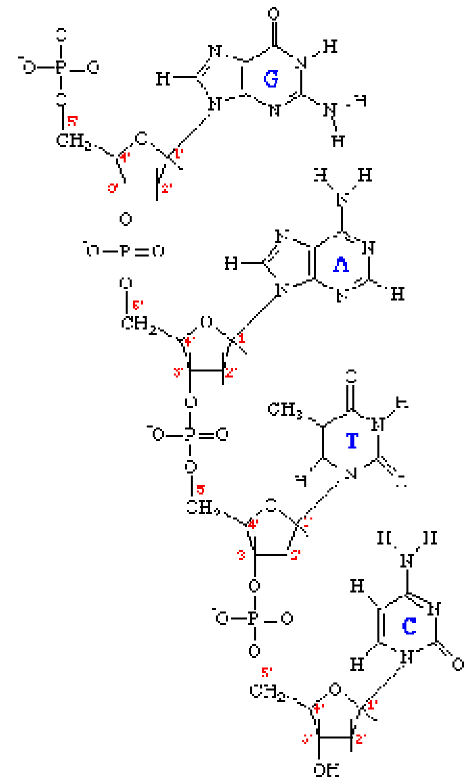
McIntosh & Saleh, PRL 09, PRE 09, Macromol. 11

a = 6.4 Å spacing between charges

l_B = 7.1 Å

electrostatic blob size

$\xi = l_0^{2/3}(a/l_B)^{2/3} \cong 1$



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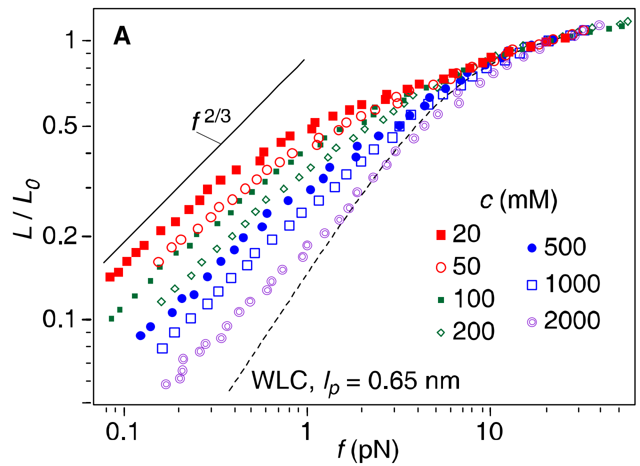
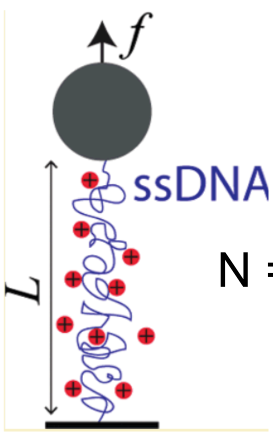
Logarithmic Scaling in Experimental Data

monovalent salt (20-2000mM)





N = 5000

divalent salt (2:1) (0.2-50mM)

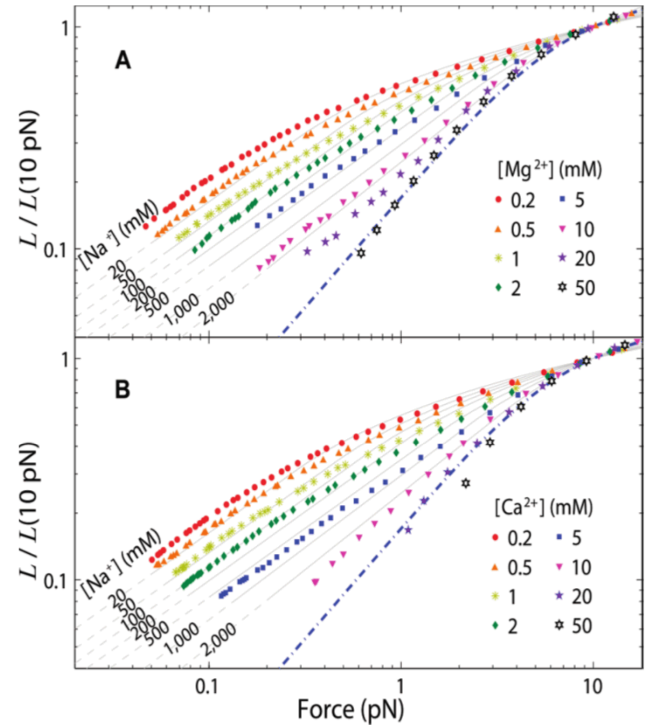


Figure 2. Force−extension behavior of d-ssDNA in 2:1 salt solutions of (A) $MgCl_2$ and (B) $CaCl_2$. For comparison, we plot gray curves in the background that represent consensus behavior in NaCl at various concentrations; the blue dash-dotted line is a WLC with persistence length 0.62 nm.

McIntosh & Saleh, PRL 09, PRE 09, Macromol. 11

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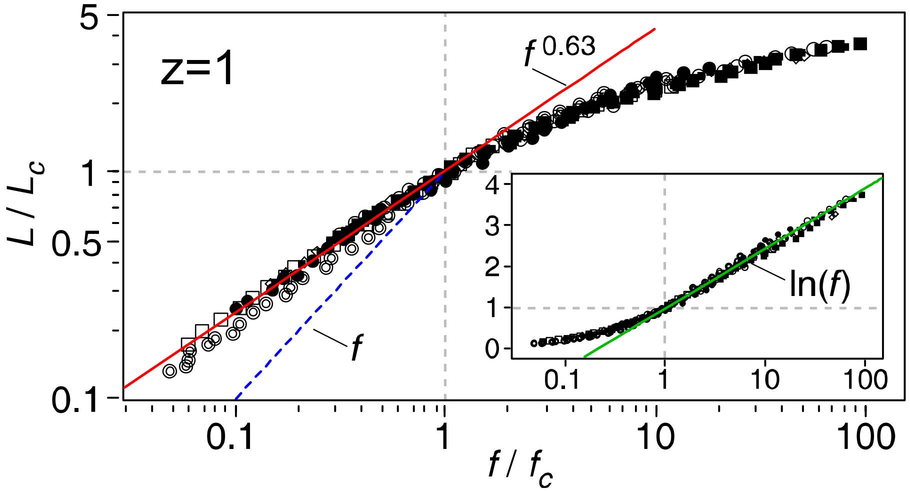
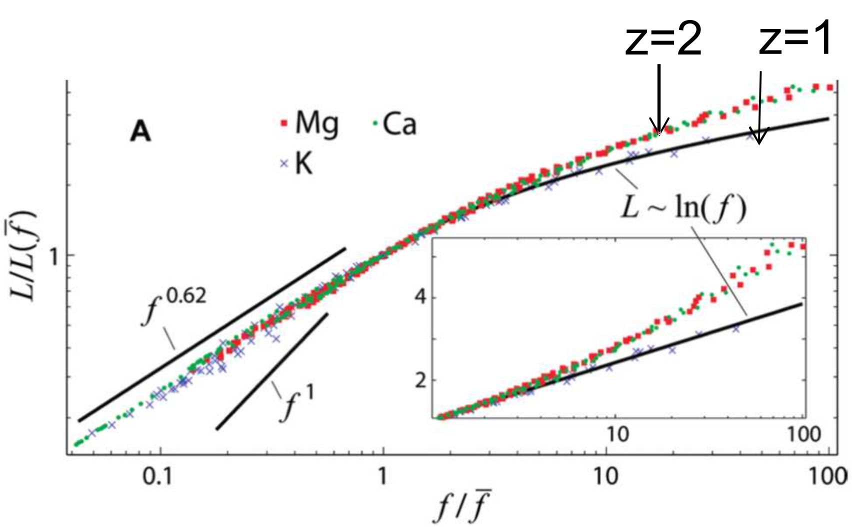
Scaling in Experiment





low f
- independent of valence, ion
- $\gamma \cong 0.62$

high f
- logarithmic scaling
- depends on valence

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MD Simulations

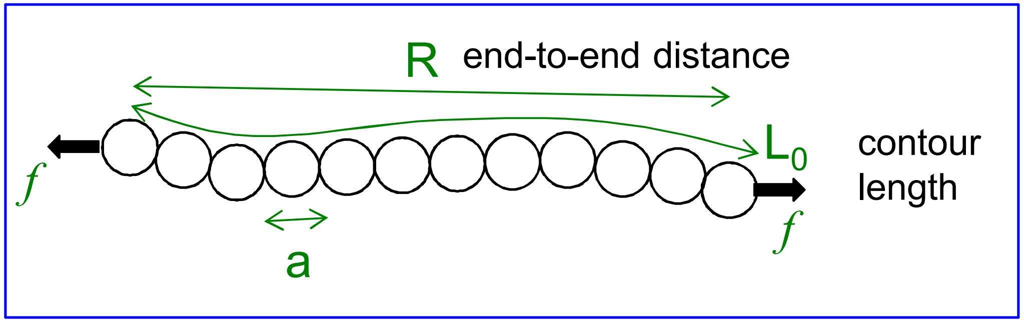
"All ion simulations"

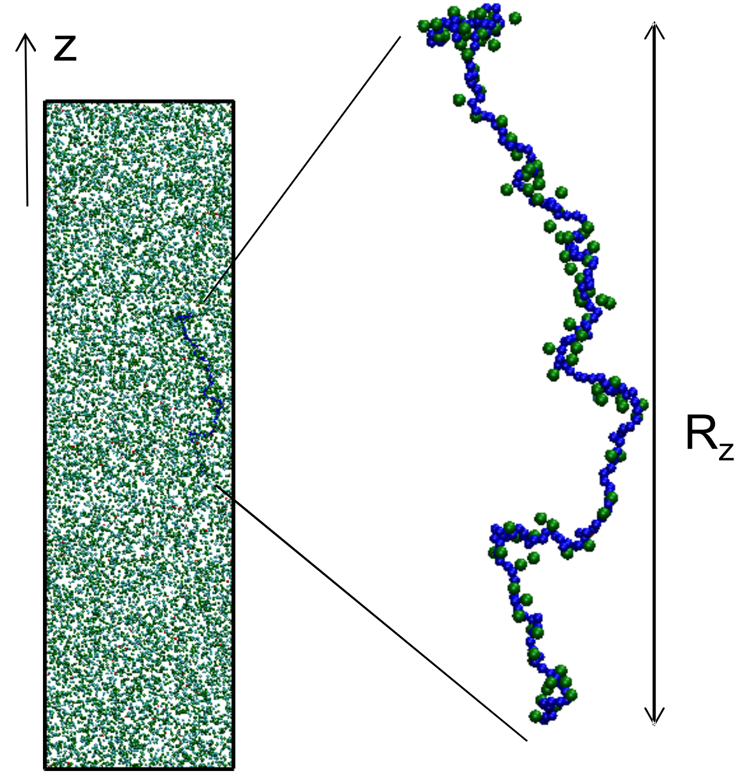
- bead (spring) flexible polyelectrolyte
- F = bond + electrostatics + entropy
- a = 6.4 Å = 0.96 σ (ssDNA spacing)
- N = 200
- monovalent, divalent salt

divalent systems are small (easy sims)

monovalent system are LARGE (expensive)

- $L_0 = (N-1)\, a = 192\, \sigma$
- $l_B = 1.065\, \sigma$ (Bjerrum length)





20 mM monovalent

$f = 0.20\ \varepsilon/\sigma$

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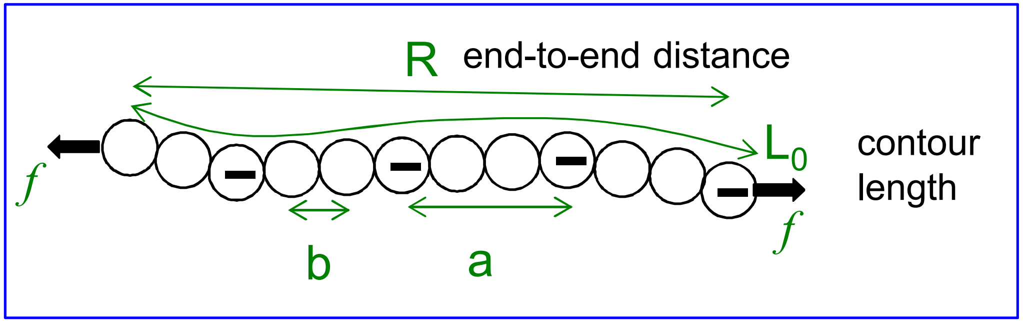
Additional Systems

- $b = 0.96\ \sigma$ bond length is fixed
- $a = m\ b$ charge spacing is varied



Intrinsic stiffness:
add angle term to potential
$k_a\ \theta^2$

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Screened Coulomb Simulations

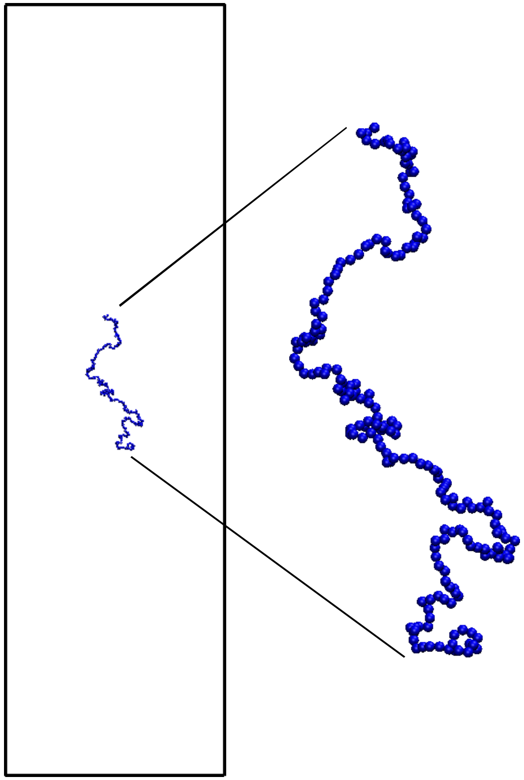
To do very low f and large N,
go to screened Coulomb potential

$$u(r) = q_i q_j \frac{e^{-\kappa r_{ij}}}{r_{ij}}$$

Only monomers present in system.
Monte Carlo simulations
  N=200, 1000, 5000, 25000
  at 200 mM
  using pivot algorithm (very efficient)

Much much faster.

Good approximation at 200 mM.
Worsens as c_s decreases.
Not even attempted for divalent.



200 mM monovalent
f = 0.20 ε/σ

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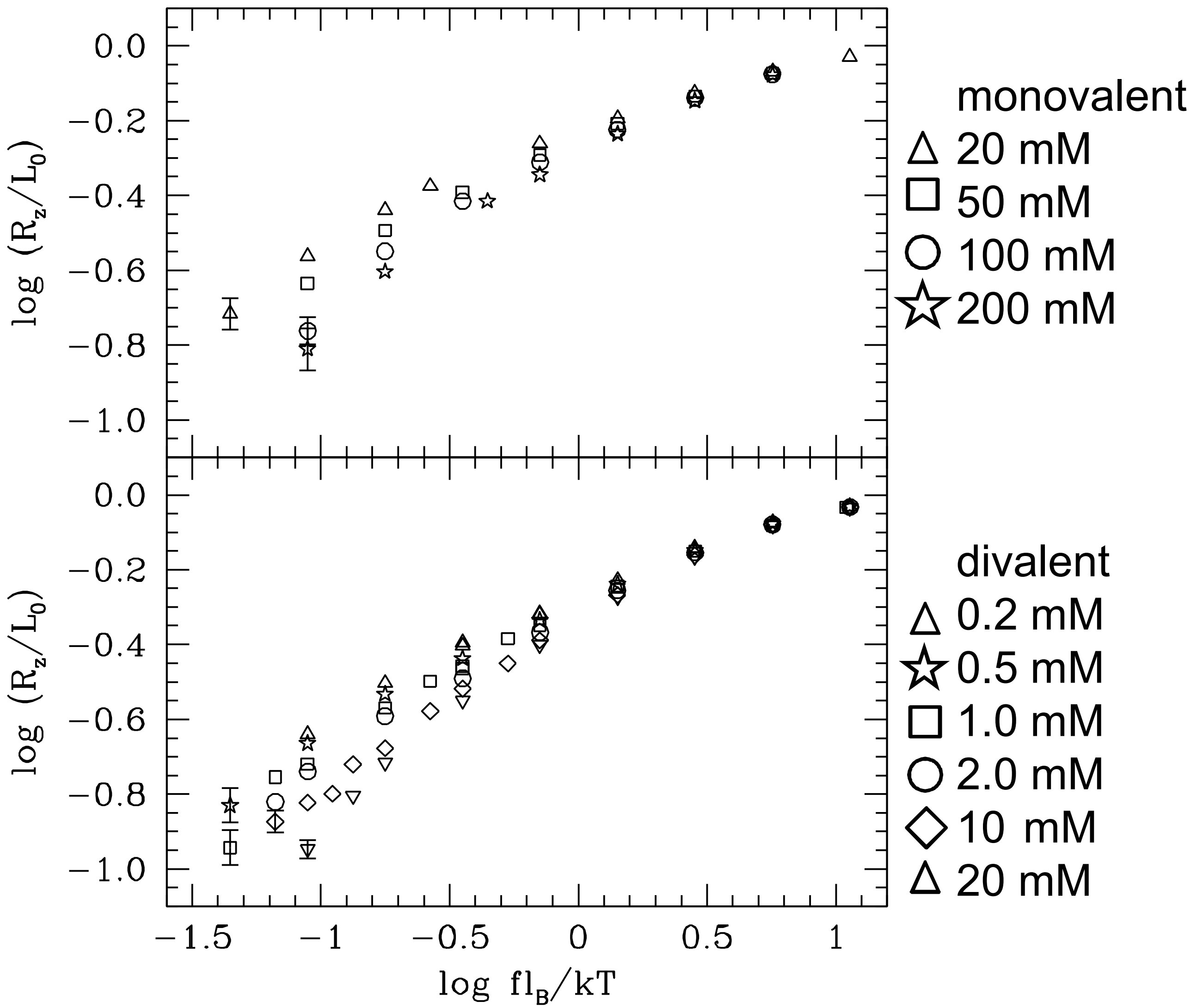
Force-Extension Data (MD)

- salt dependence
  - valence
- high force overlap

- no bond stretch until $f = 12\ \varepsilon/\sigma$ (last pt.)



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Scaling of Simulation Data

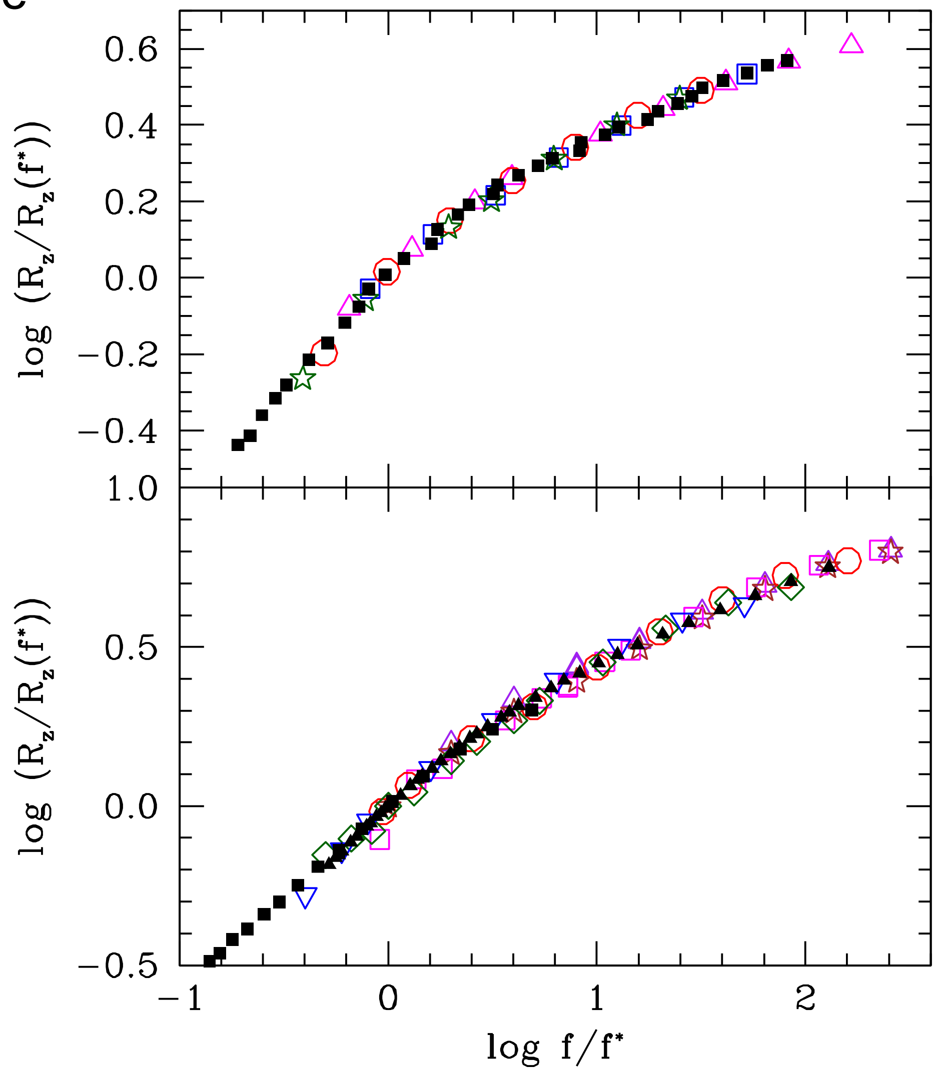
same scaling procedure as experiments

$f_c, L_c \leftrightarrow f^*, L^* \leftrightarrow \bar{f}, \bar{L}$

(notation varies)

Implies simple model is sufficient.

electrostatics, entropy, connectivity



monovalent
- 20 mM
- 50 mM
- 100 mM
- 200 mM

experimental data solid points

divalent
- 0.2 mM
- 0.5 mM
- 1.0 mM
- 2.0 mM
- 10 mM
- 20 mM

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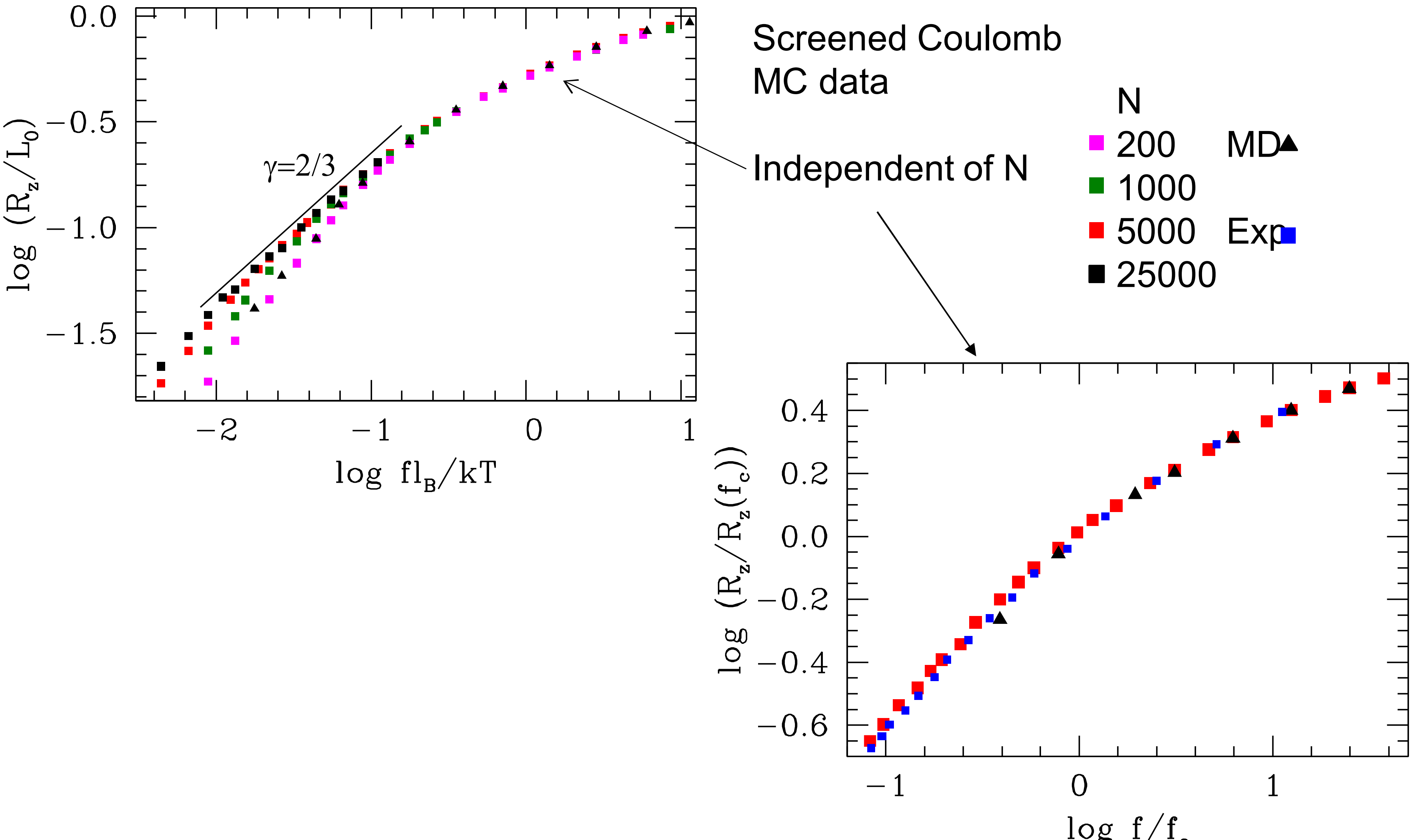
N=5000 200mM



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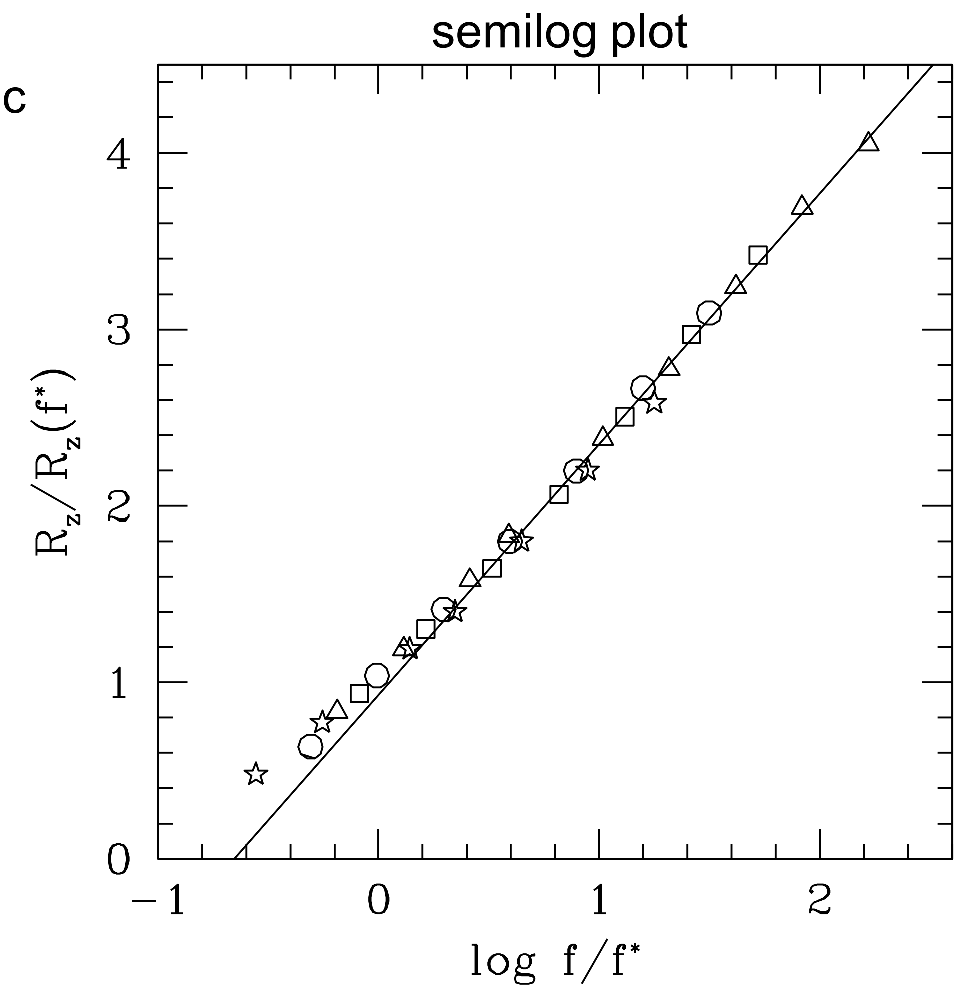
Logarithmic regime (monovalent)

Clearly have logarithmic regime at large f.

MD, all ion simulations N=200 data

In fact, most f are in logarithmic.



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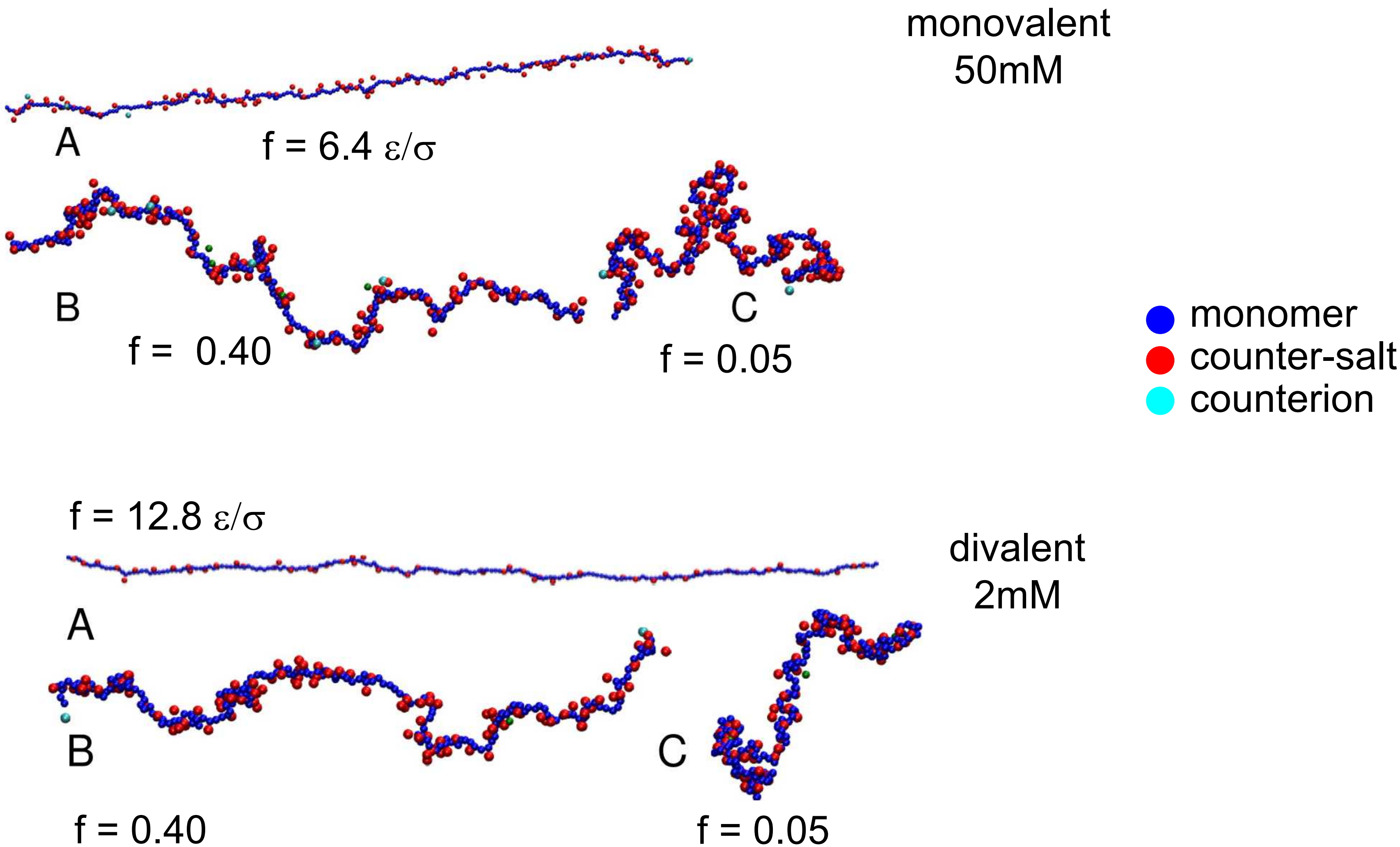
Structure



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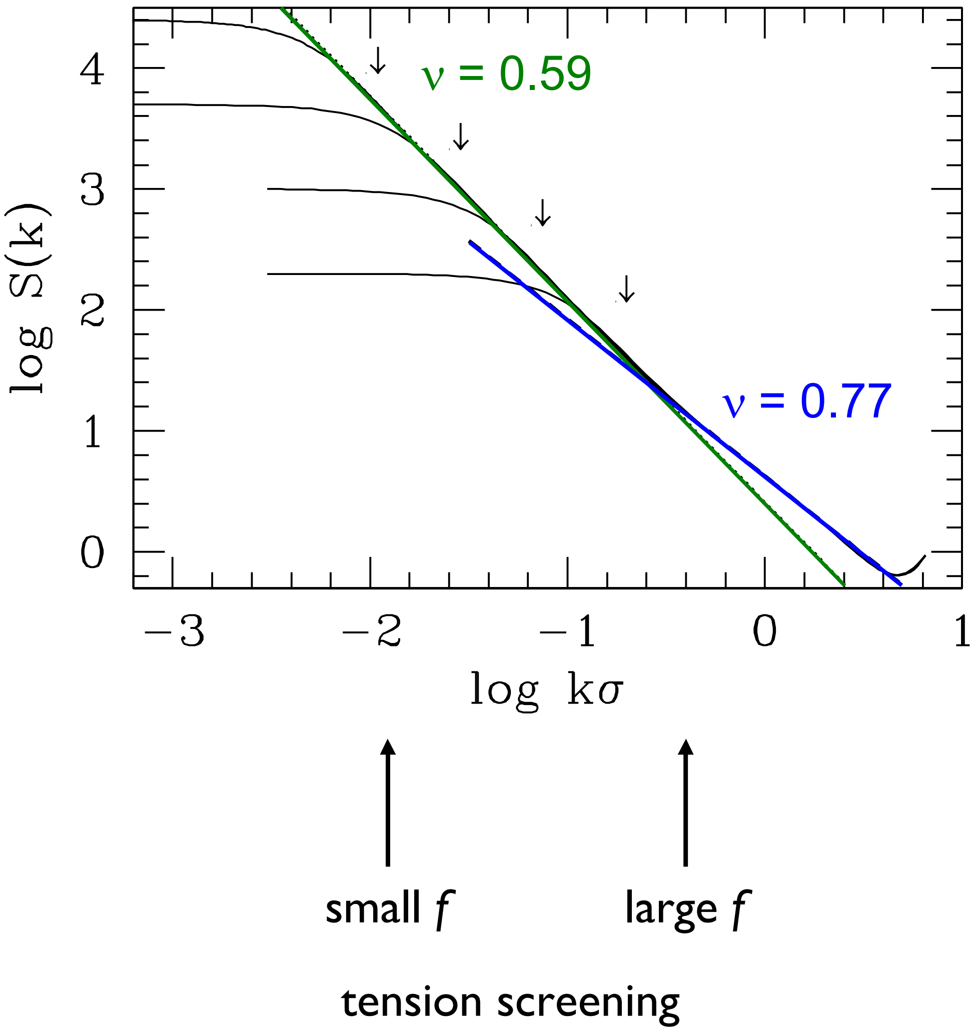
S(k) & Chain Length Dependence

- Screen Coulomb Simulations
  - true with explicit ions at smaller N
- N = 200, 1000, 5000, 25000
- S(k) same for k > 2π/R(N)
- two regimes
- f=0

Large f depends on high k regime and does not depend on N.
<u>Can do with all ion MD at N=200.</u>

Low f regime requires large N.
MC simulations at 200 mM:

Debye length = 1 σ
r_c = 5.57 σ
r = 10 σ at log kσ = -0.5



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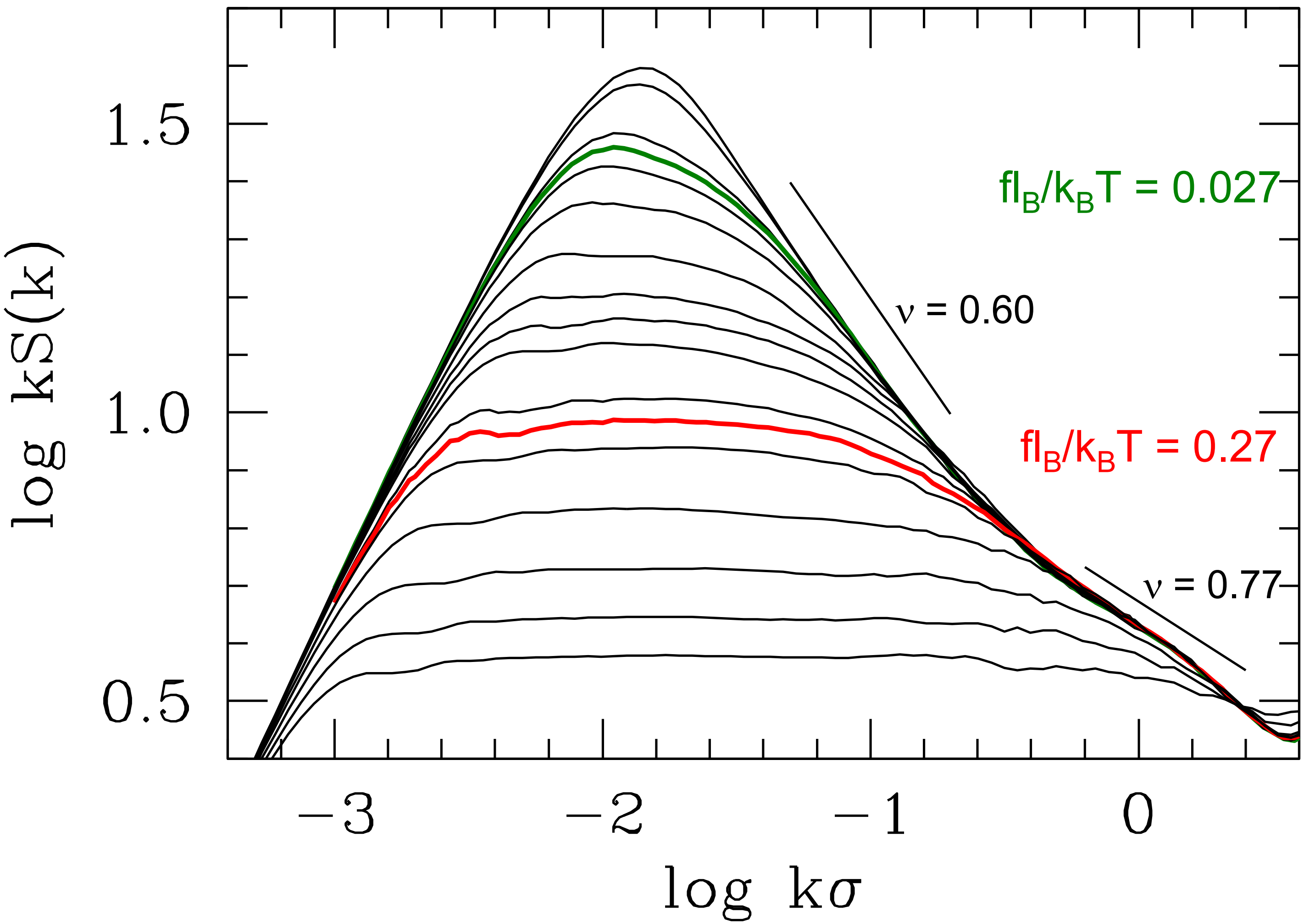
Structure Factor for N=5000 at 200 mM



<u>Region</u>

Rotational

Pincus

logarithmic

at high f,
affects large k
structure
ν=0.77 ¯3/5

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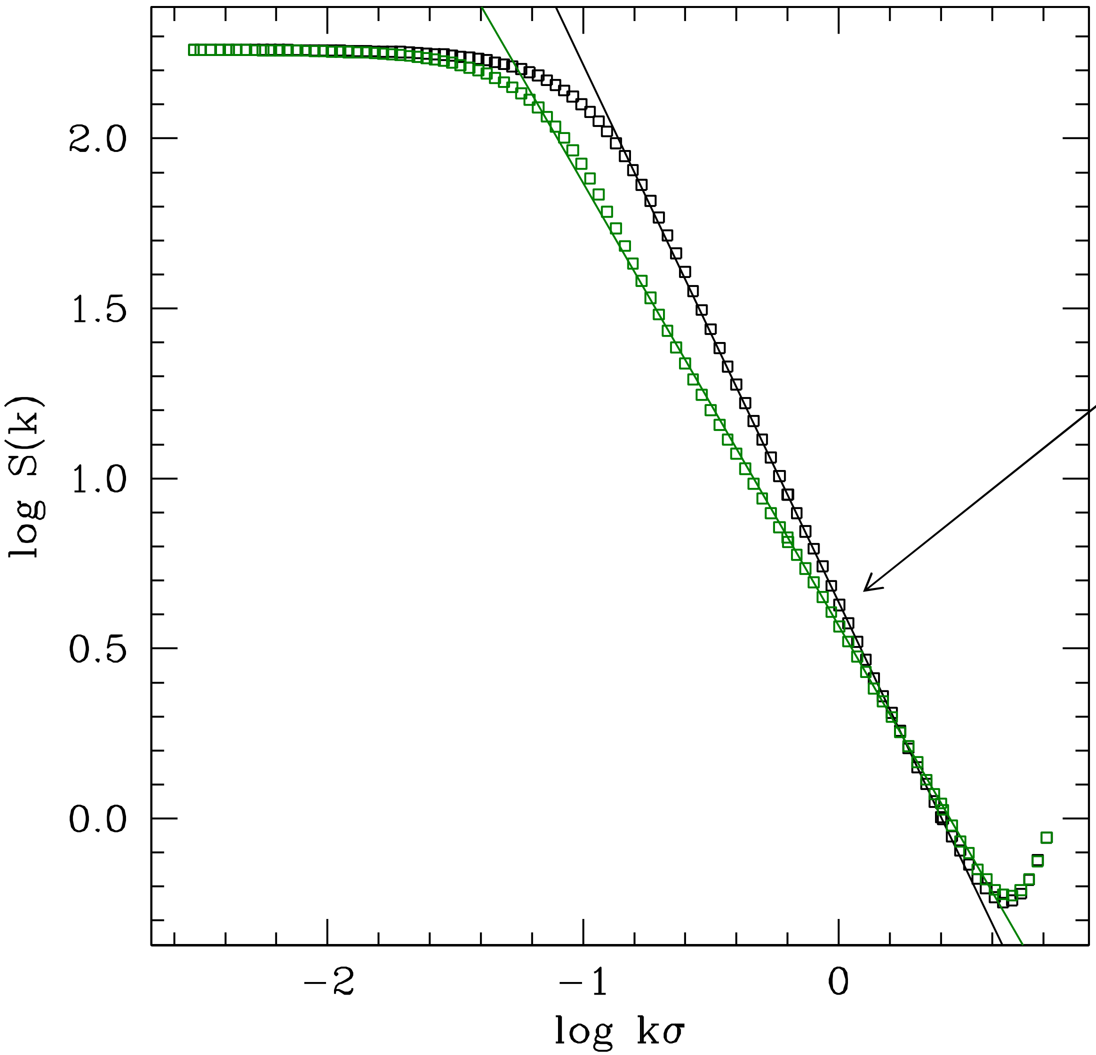
S(k) comparison for z=1 and 2 at f = 0



N=200 at 50 mM

$S(k) \sim k^{1/\nu}$

high k

z=1 ν=0.77 (green)

z=2 ν=0.63 (black)

Structural difference leads to different scaling in force-extension.

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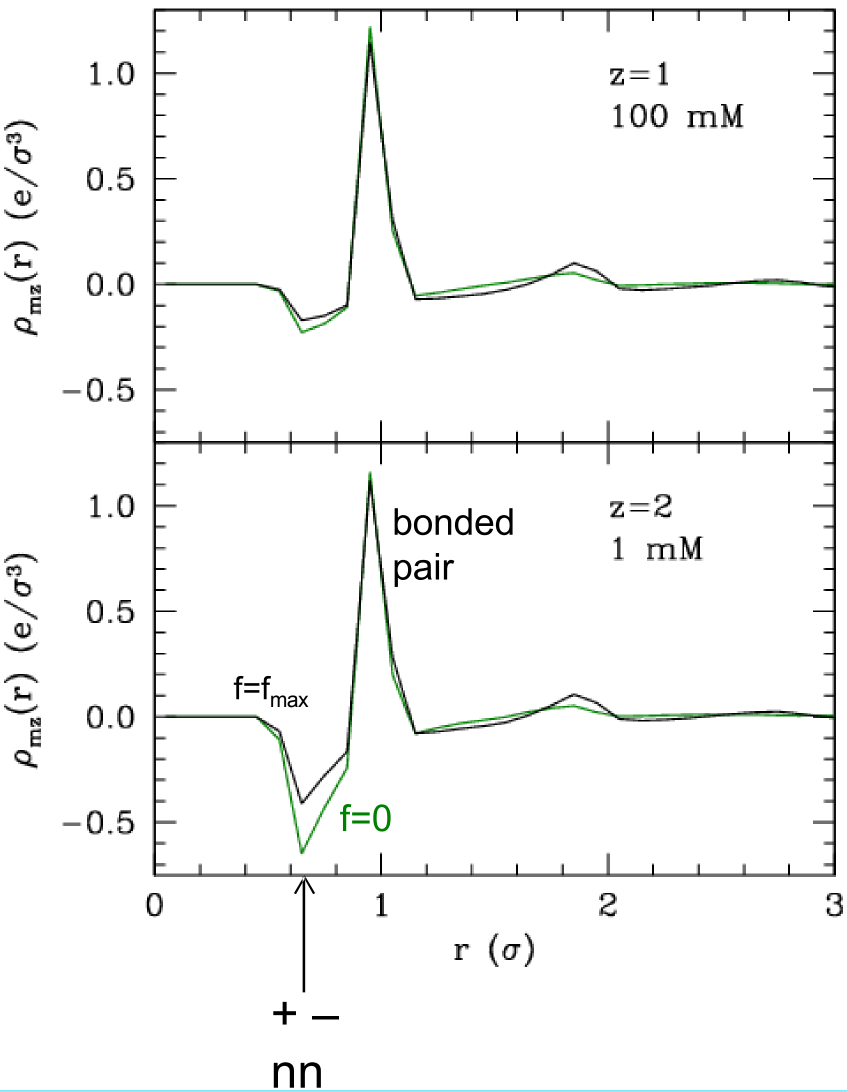
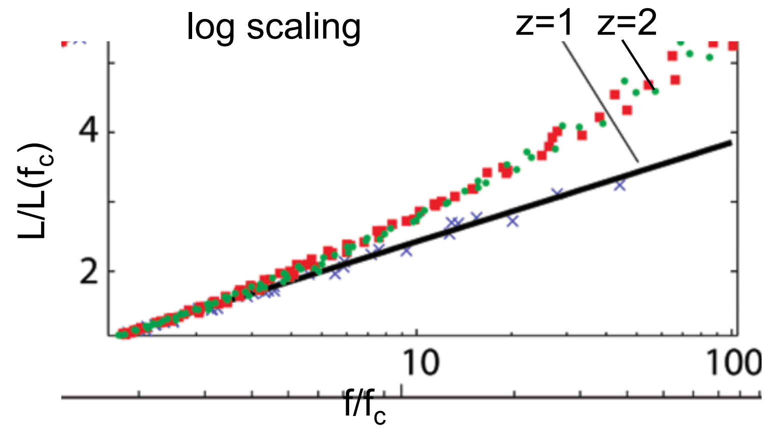
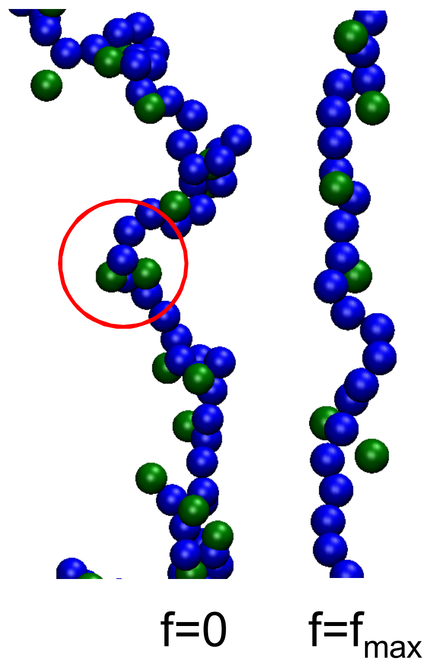
Why Divalent Different

Charge Density about Monomer







Chain curls around divalent counterions

- smaller ν
- larger negative trough
- larger change at max f

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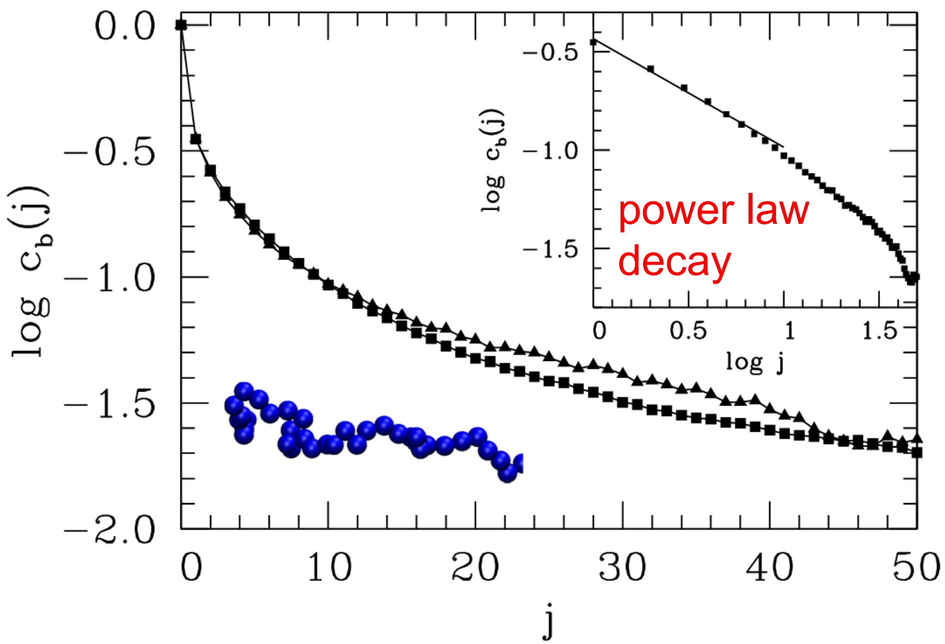
Bond-bond correlation function

$$c_b(j) = \langle b_i \bullet b_{i+j} \rangle \sim \exp\left(\frac{j}{L_p}\right)$$

▲ N=200 at 200 mM (MD)
■ N=5000 (MC)



This nonexponential decay has been known since the 90s.

The force-extension data shows it has important implications.

Toan & Thirumalai JCP 2012
$c_b(j) \sim (j/a)^{-\alpha} \Rightarrow R \sim \ln(f)$

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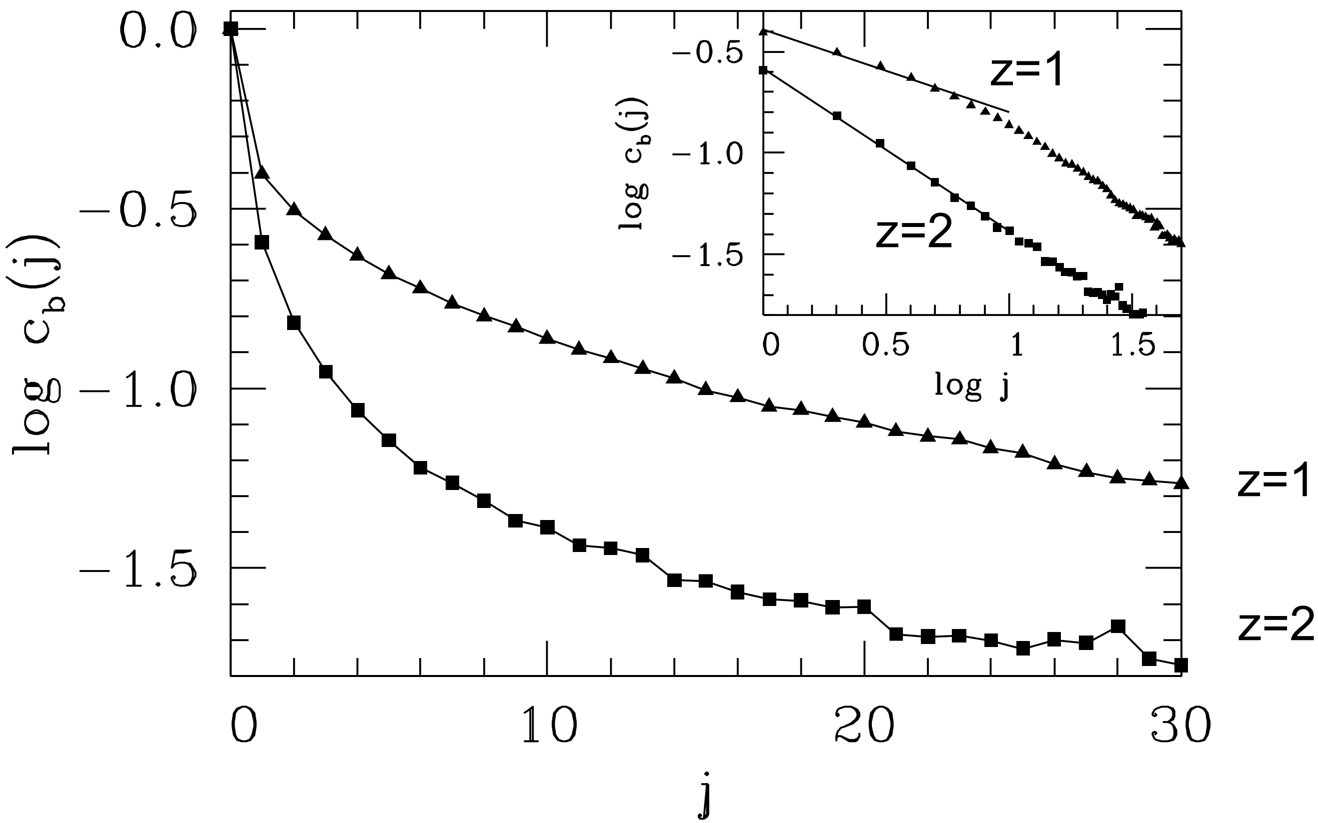
bond-bond for z=1 & 2

- bond-bond correlation different at small separations for 50 mM at f=0
- algebraic at small separations
- slopes -0.41 and -0.80 for z=1 and 2, resp.



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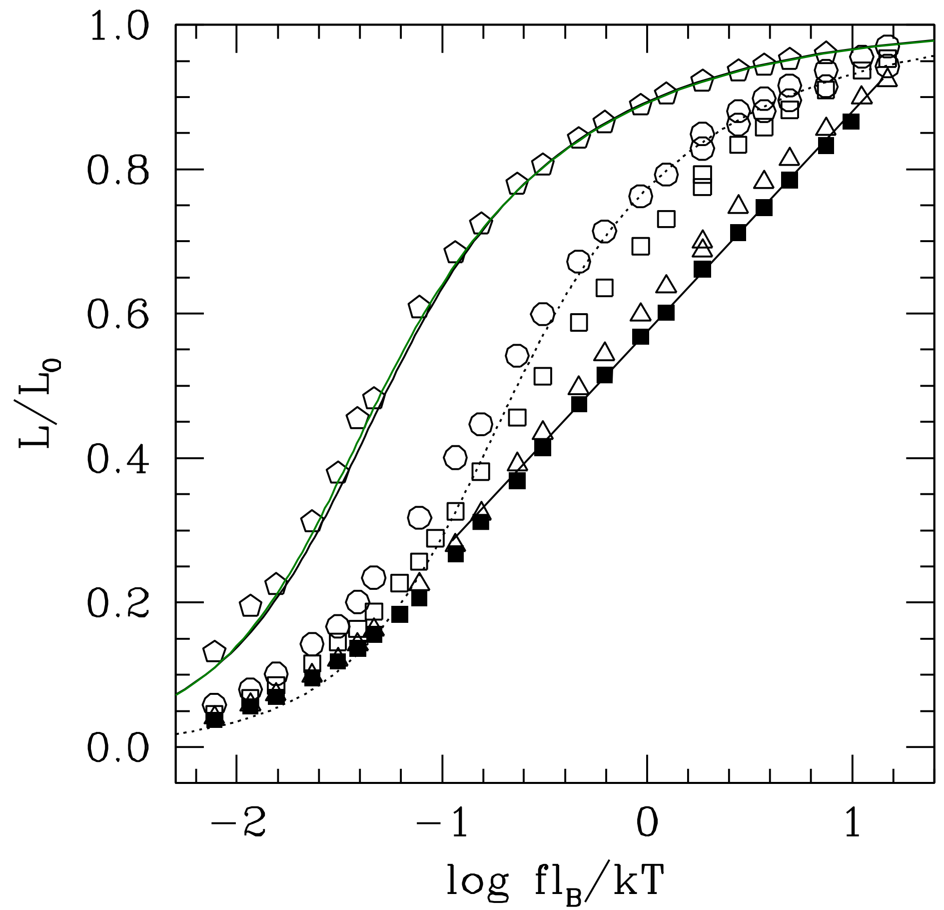
Intrinsic Stiffness Removes Log Regime

- MC simulations varying stiffness at 200 mM
- k_a = ■0, △1, □5, ○10, ⬠50



Marko-Siggia curves

.... $k_a = 10$

——— $k_a = 50$

Wormlike chain model good fit at $k_a = 50$ ($k_a = 42\ k_BT$)

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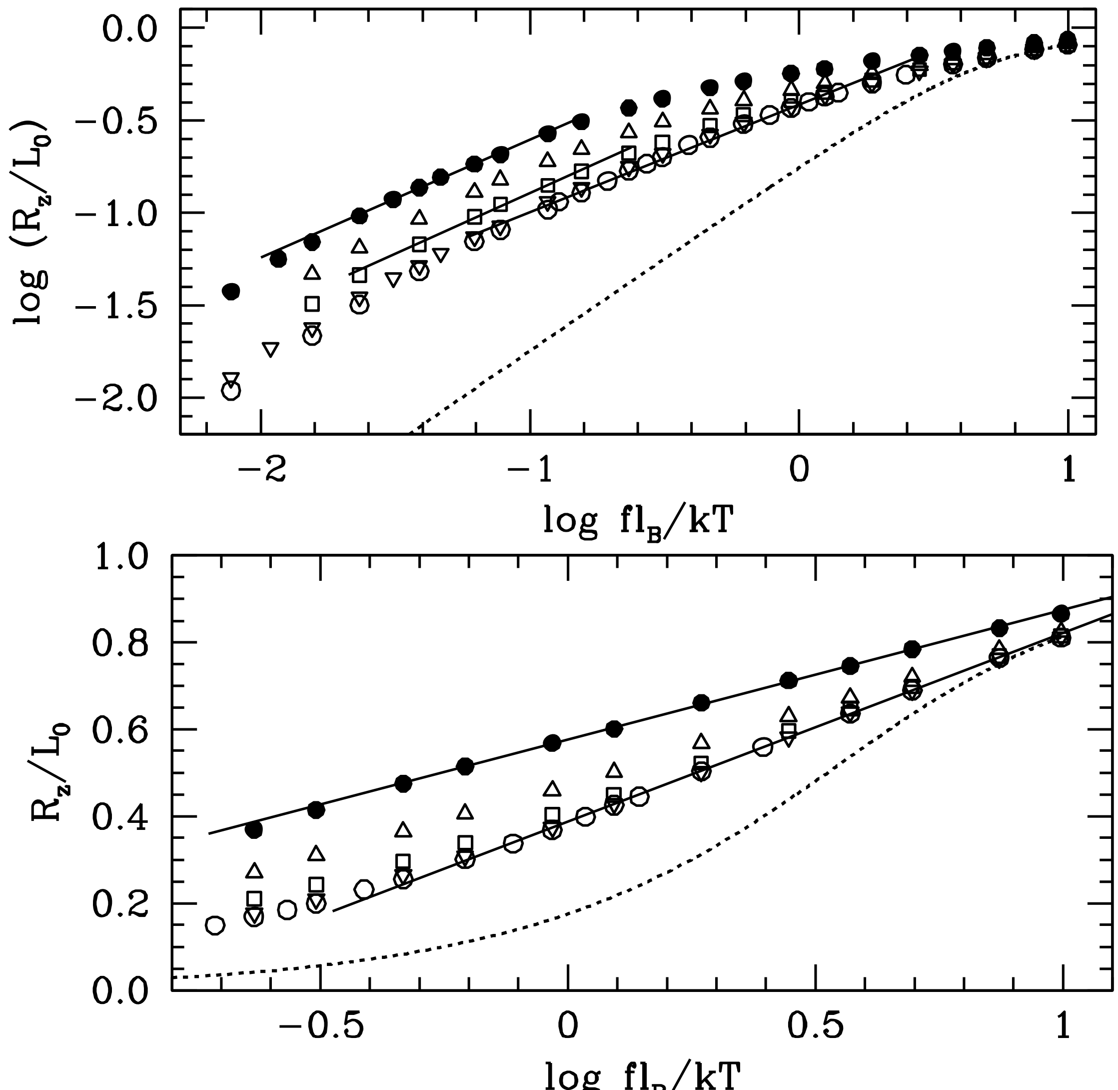
Varying Charge Separation

a=b, 2b, 4b, 10b, ∞

FJC

200 mM
N=5000



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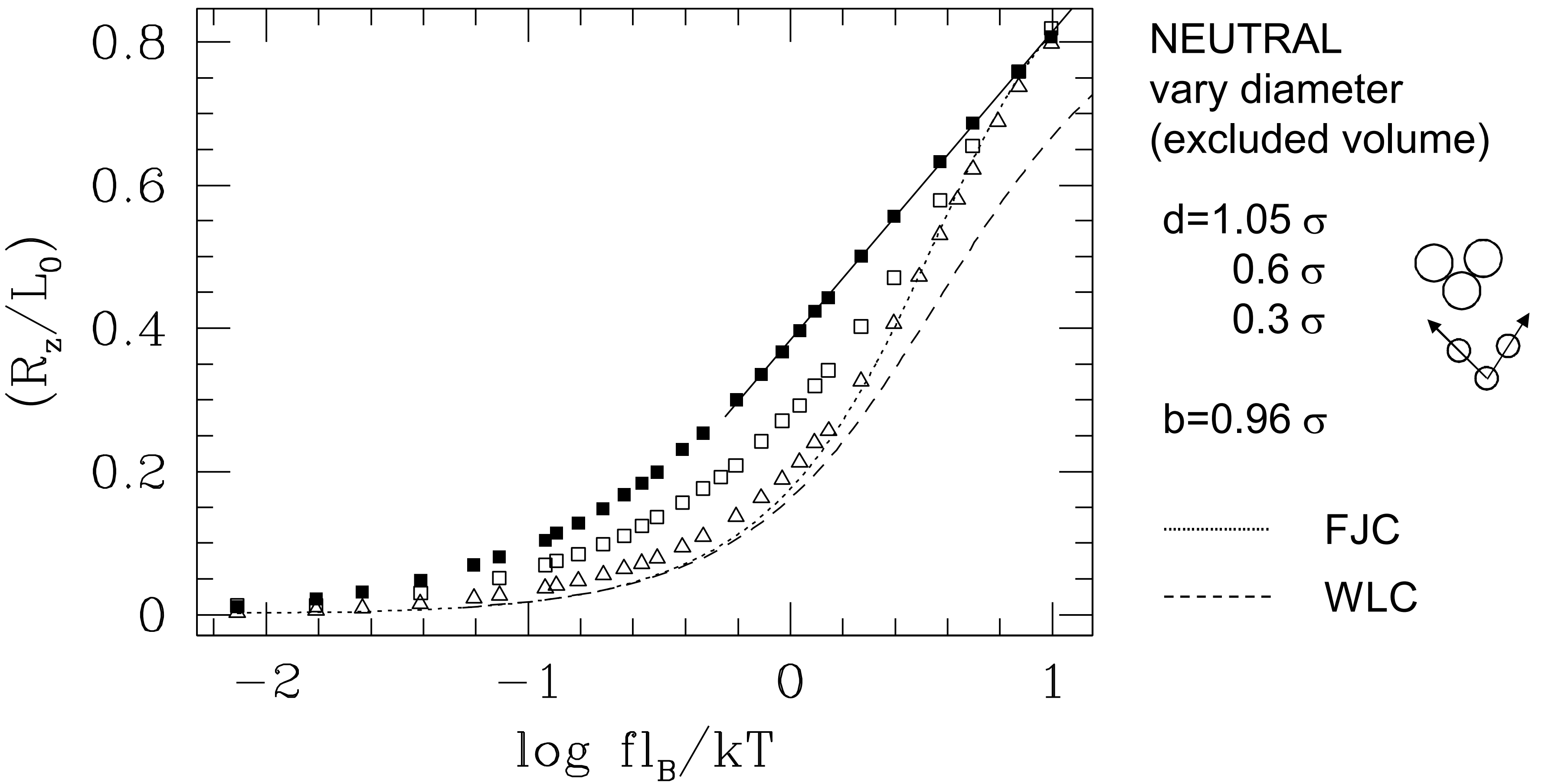
Do you need charges to get logarithmic regime?



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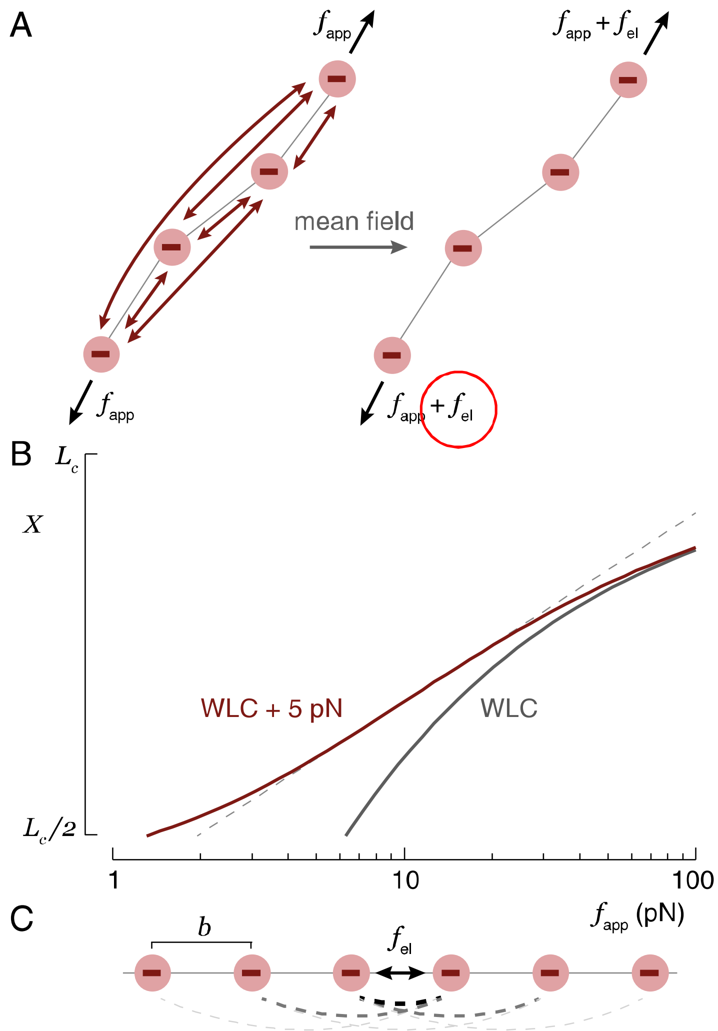
Internal Tension Model



for the intermediate force regime

$$X = L_c\left(1 - \sqrt{\frac{k_B T}{4 l_p (f_{\rm app} + f_{\rm el})}}\right),$$

f_{el} is related to electrostatic tension

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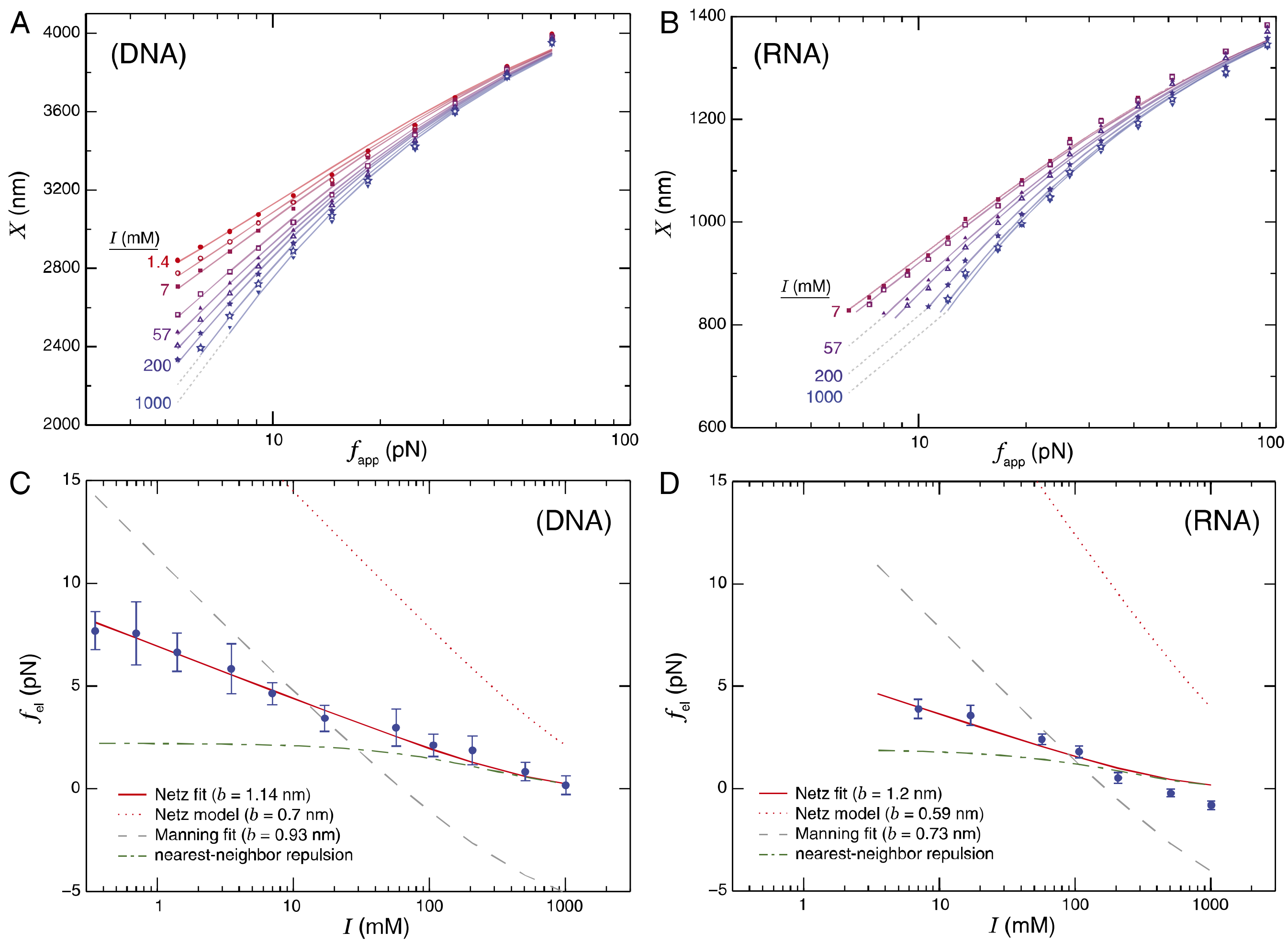
ssDNA & ssRNA data



f_{el} is obtained by fitting data

PNAS, 2017

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Conclusions

- Can reproduce key aspects of experiments
  - scaling due to added salt (monovalent, divalent)
  - logarithmic regime
  - Pincus regime
  - reproduce experimental findings
- Structural insight to stretched, flexible polyelectrolyte
  - force screening
  - sequence: orient, unfold, unwrinkle
  - logarithmic regime is due to unwrinkling
    - bond-bond power law
    - does not require electrostatics
- Picture of flexible polyelectrolyte
  - new mean-field like force-extension equation

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Publications

- D.R. Jacobson, D.B. McIntosh, M.J. Stevens, M. Rubinstein, and O.A. Saleh. "Single-stranded nucleic acid elasticity arises from internal electrostatic tension." Proceedings of the National Academy of Sciences 114 (2017): 5095-5100.
- M.J. Stevens, and O.A. Saleh. "Simulations of stretching a flexible polyelectrolyte with varying charge separation." The European Physical Journal Special Topics 225 (2016): 1683-1692.
- M.J. Stevens, D.B. McIntosh, and O.A. Saleh. "Simulations of stretching a strong, flexible polyelectrolyte: Using long chains to access the Pincus scaling regime." Macromolecules 46 (2013): 6369-6373.
- M.J. Stevens, D.B. McIntosh, and O.A. Saleh. "Simulations of stretching a strong, flexible polyelectrolyte." Macromolecules 45 (2012): 5757-5765.

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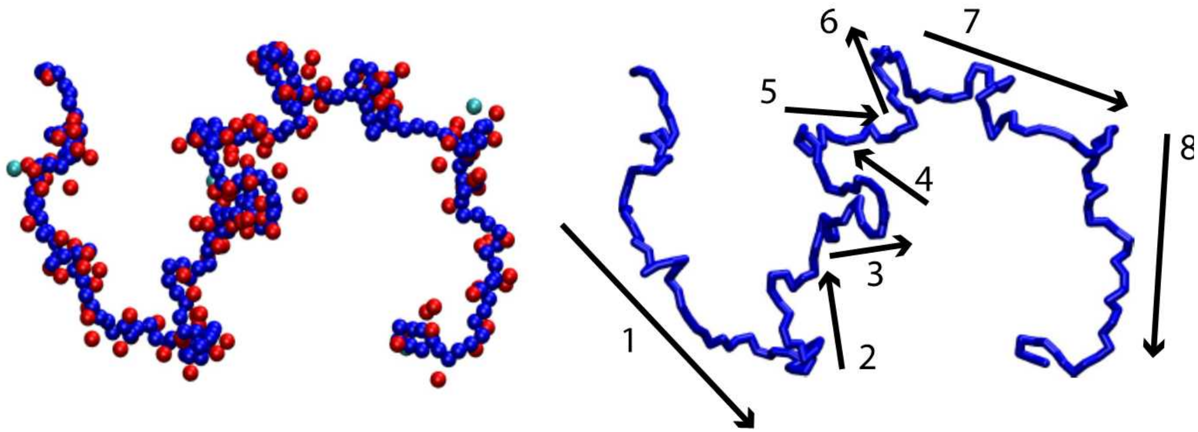
What's the Picture of Stetching Polyelectrolyte

Folds & Condensed Counterions



monovalent
50 mM
f = 0.05 ε/σ

~ 8 folds

Large & Short length scales
Folds ~ persistence length segments
net repulsive
Wrinkles:
short length scale structure
entropy & counterion-monomer wrapping
stretched at large f
the dominate source of the logarithmic scaling
power law bond-bond yield logarithmic scaling (Toan & Thirumalai)

$k_B T/\kappa^{-1} \lesssim f_{\text{app}} \lesssim f_{\text{el}}$

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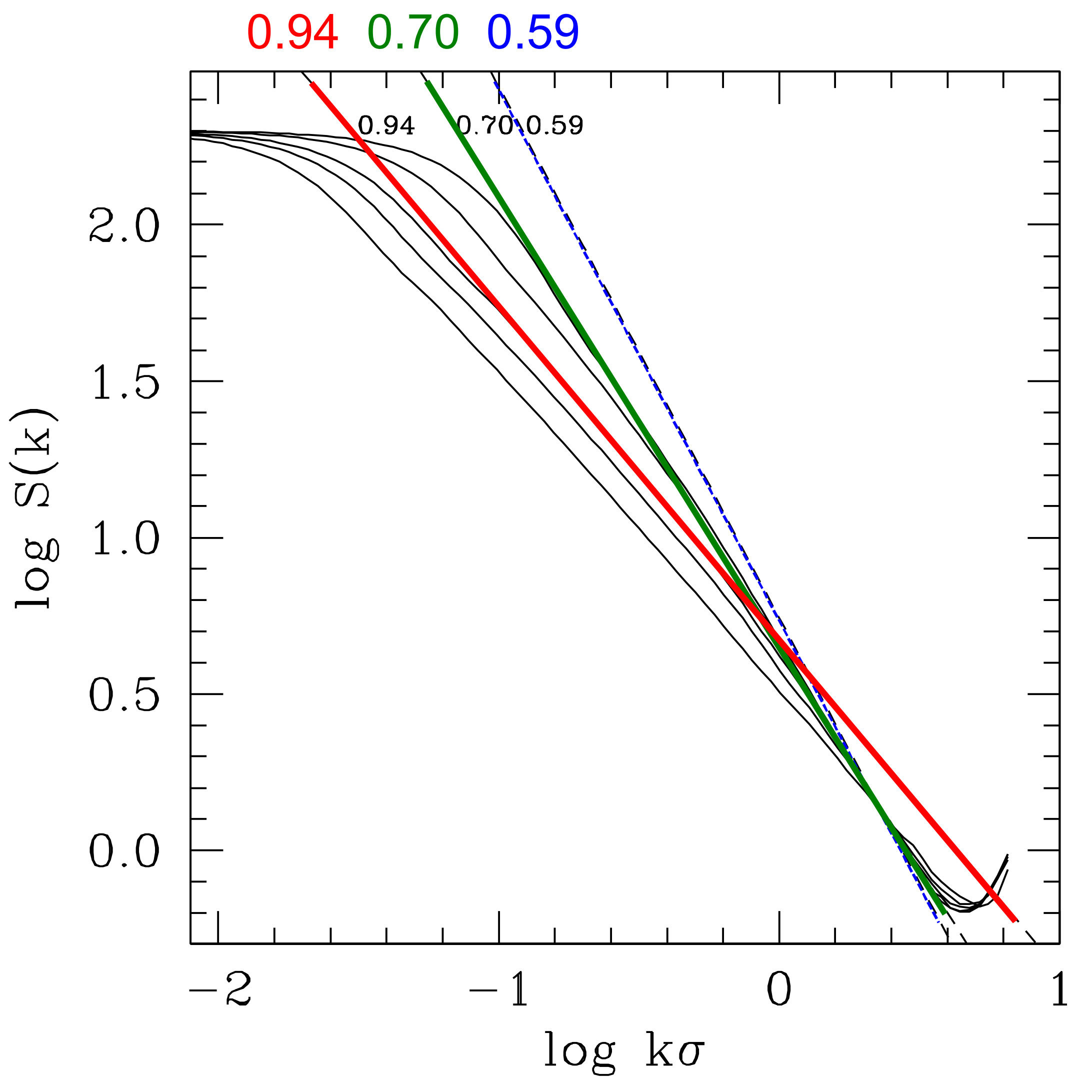
Structure Factor: force dependence



Divalent
2 mM

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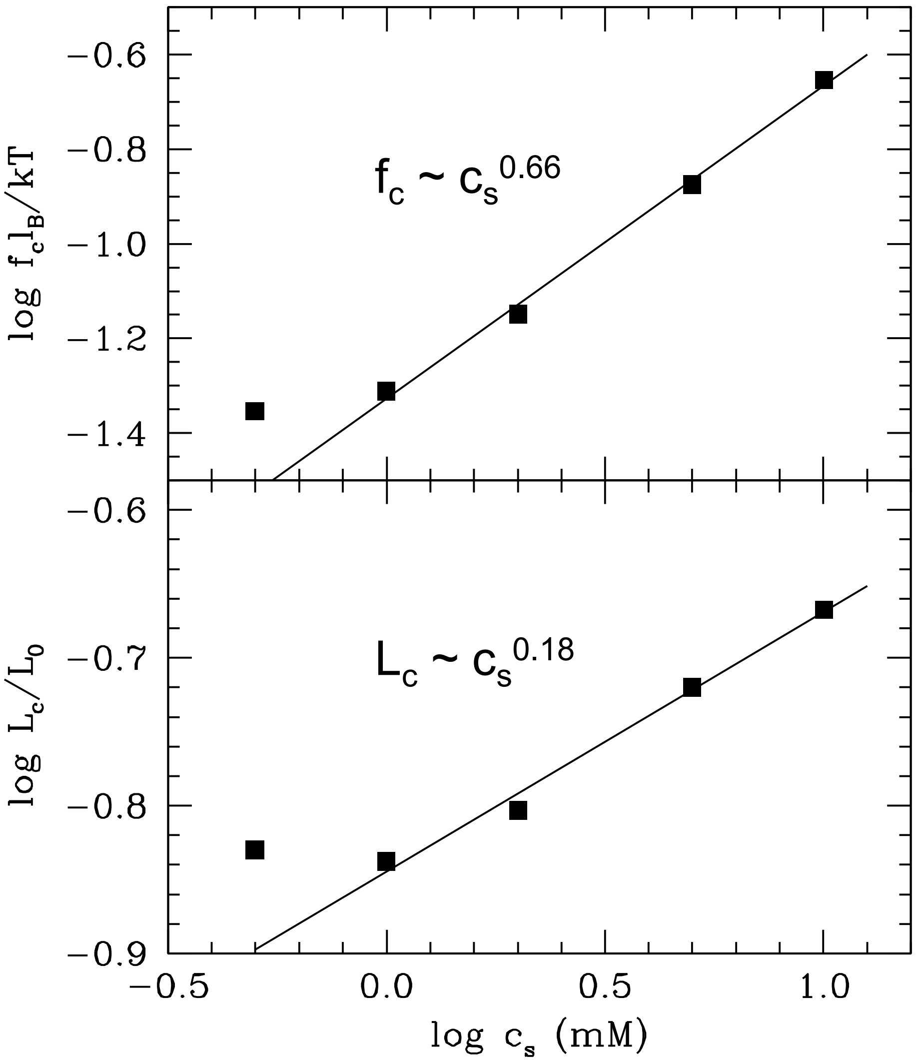
f_c & L_c scaling: Divalent



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Screened Coulomb Simulations

Most of monovalent data is in logarithmic regime.

To do better at low f (and large N),

go to screened Coulomb potential

$$u(r) = q_i q_j \frac{e^{-\kappa r_{ij}}}{r_{ij}}$$

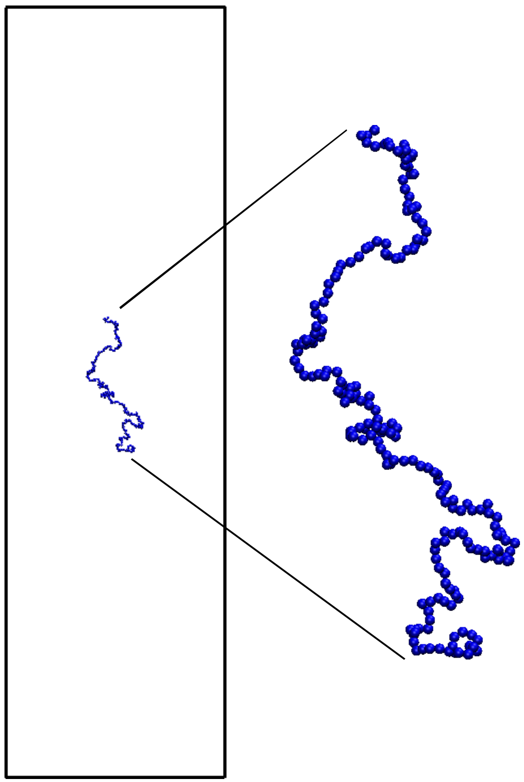
Only monomers present in system.

Much much faster.

Good approximation at 200 mM

Worsens as c_s decreases.

Not even attempted for divalent.



200 mM monovalent

$f = 0.20\ \varepsilon/\sigma$

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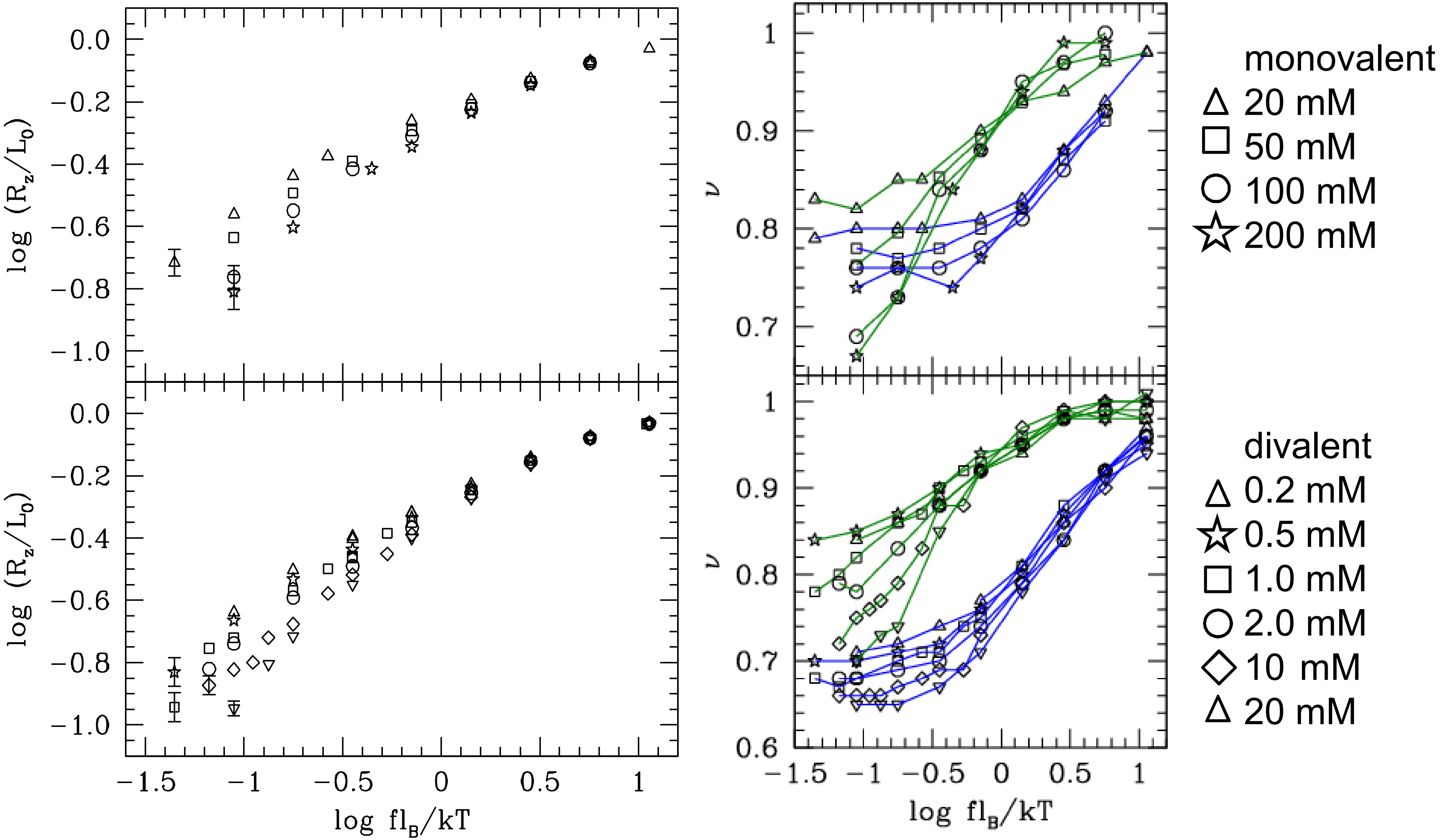
Structure:Force:Extension



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Structure Factor: scaling exponents

f = 0

salt dependence
ν decreases with c_s

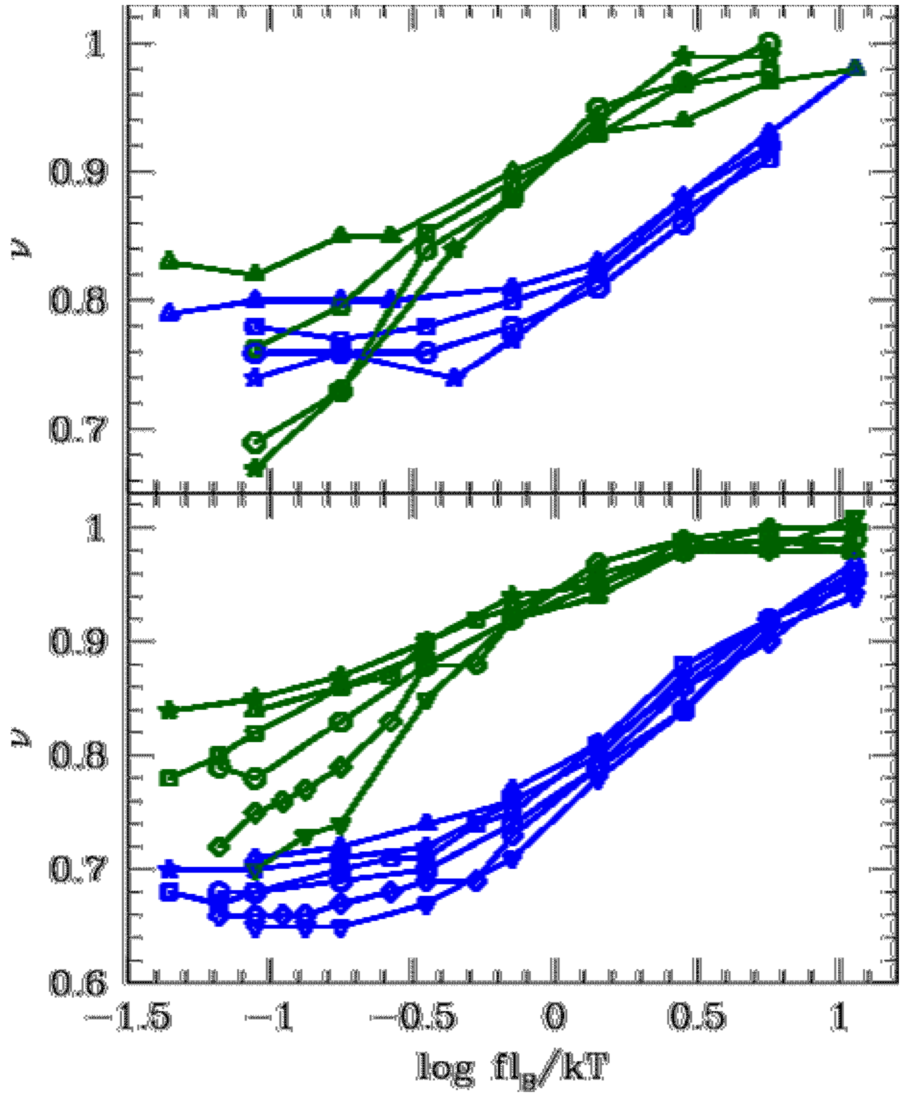
valence dependence
ν smaller for z = 2

dependence on force

high k:
ν_h constant as f → 0
fl_B/kT >0 rises close to 1

low k:
ν_l increases from low f
~identical for salt
= 1 at large f

ν_h rises once ν_l ~ 0.90



monovalent
Δ 20 mM
□ 50 mM
○ 100 mM
☆ 200 mM

divalent
Δ 0.2 mM
☆ 0.5 mM
□ 1.0 mM
○ 2.0 mM
◇ 10 mM
Δ 20 mM

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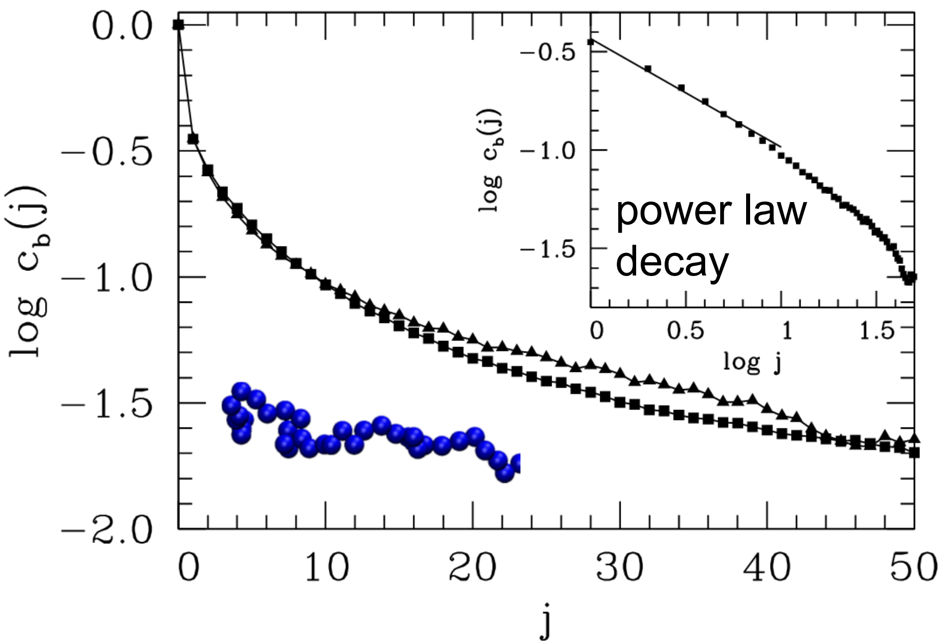
Bond-bond correlation function

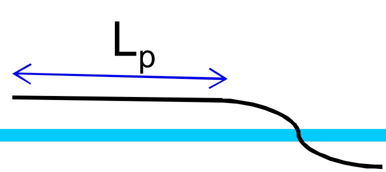
$$c_b(j) = \langle b_i \bullet b_{i+j} \rangle \sim \exp\left(\frac{j}{L_p}\right)$$

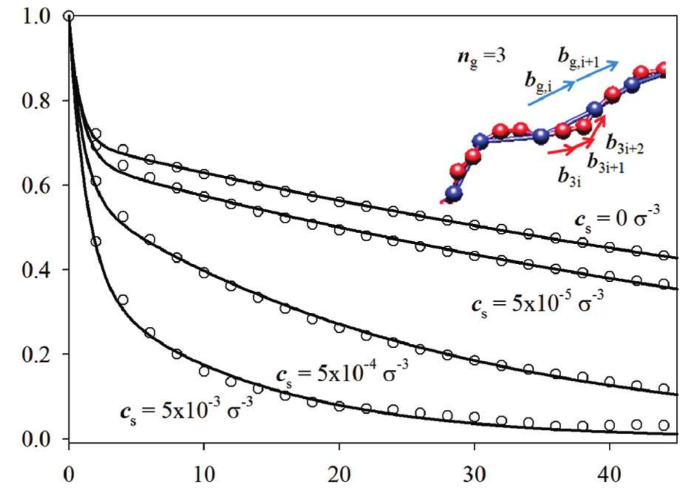
▲ N=200 MD data

■ N=5000 MC data

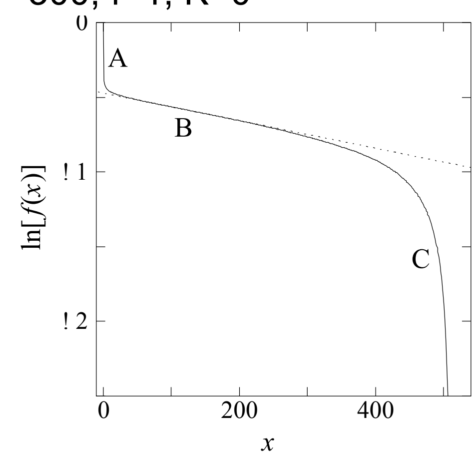


Not a WLC





Carrillo and Dobrynin (2011)
N = 300, f=1, K=0



Nguyen and Shklovskii (2002)
N = 512 @ L_D = 50 l_B

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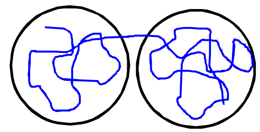
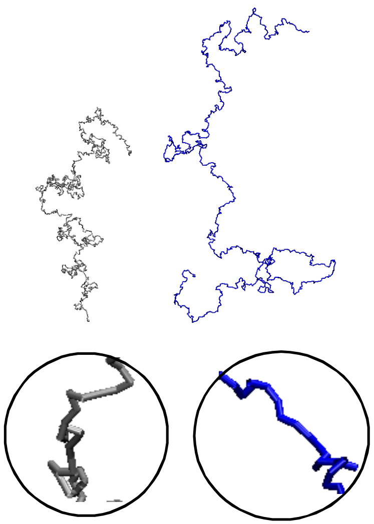
Crossover regime

electrostatic blob size
$\xi = l_0^{2/3}(a/l_B)^{2/3} \cong 1$



g,q

$$\frac{q^2}{\varepsilon \xi} = kT$$



neutral
charged

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