Runaway Transition in Irreversible Polymer Condensation with Cyclisation

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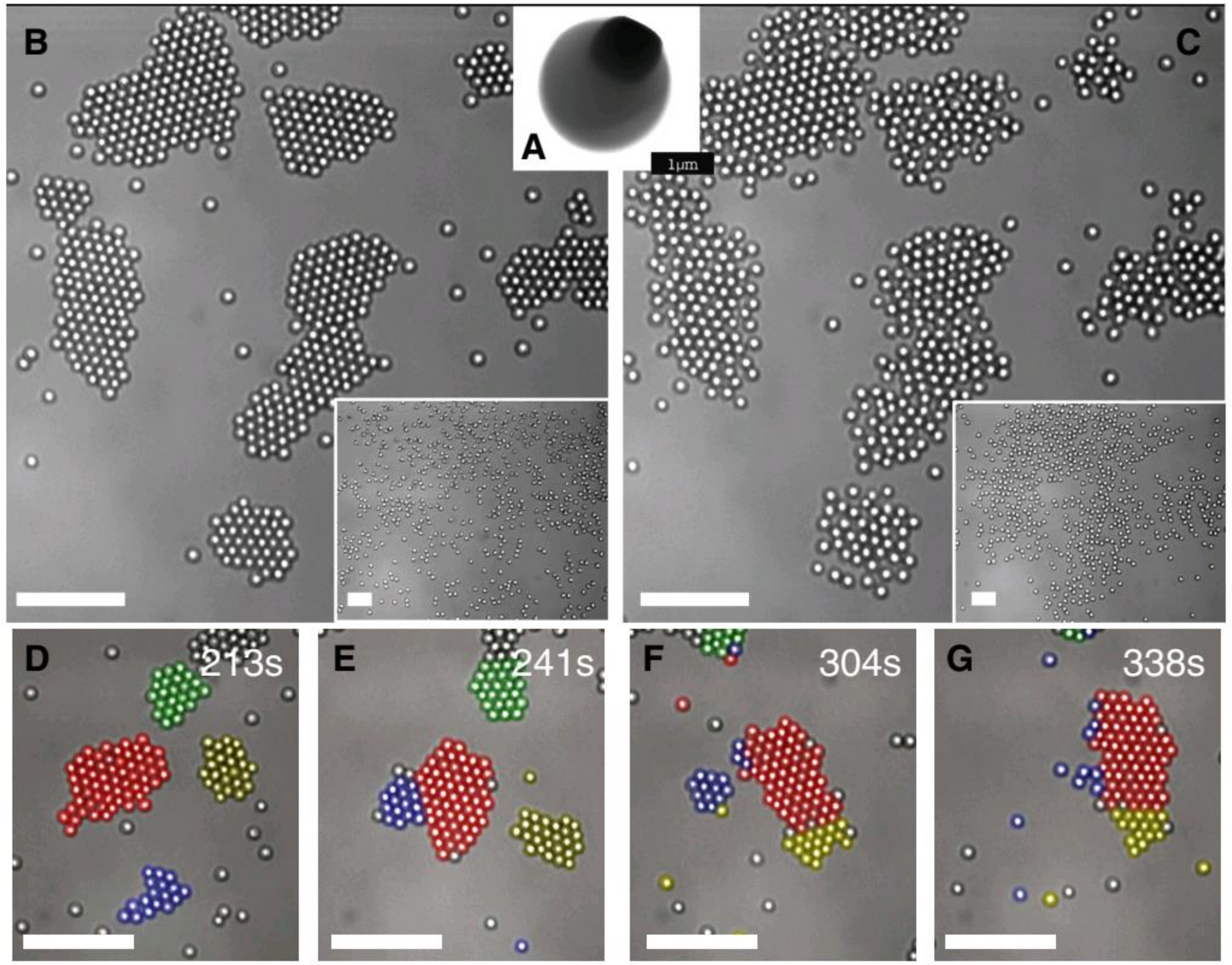
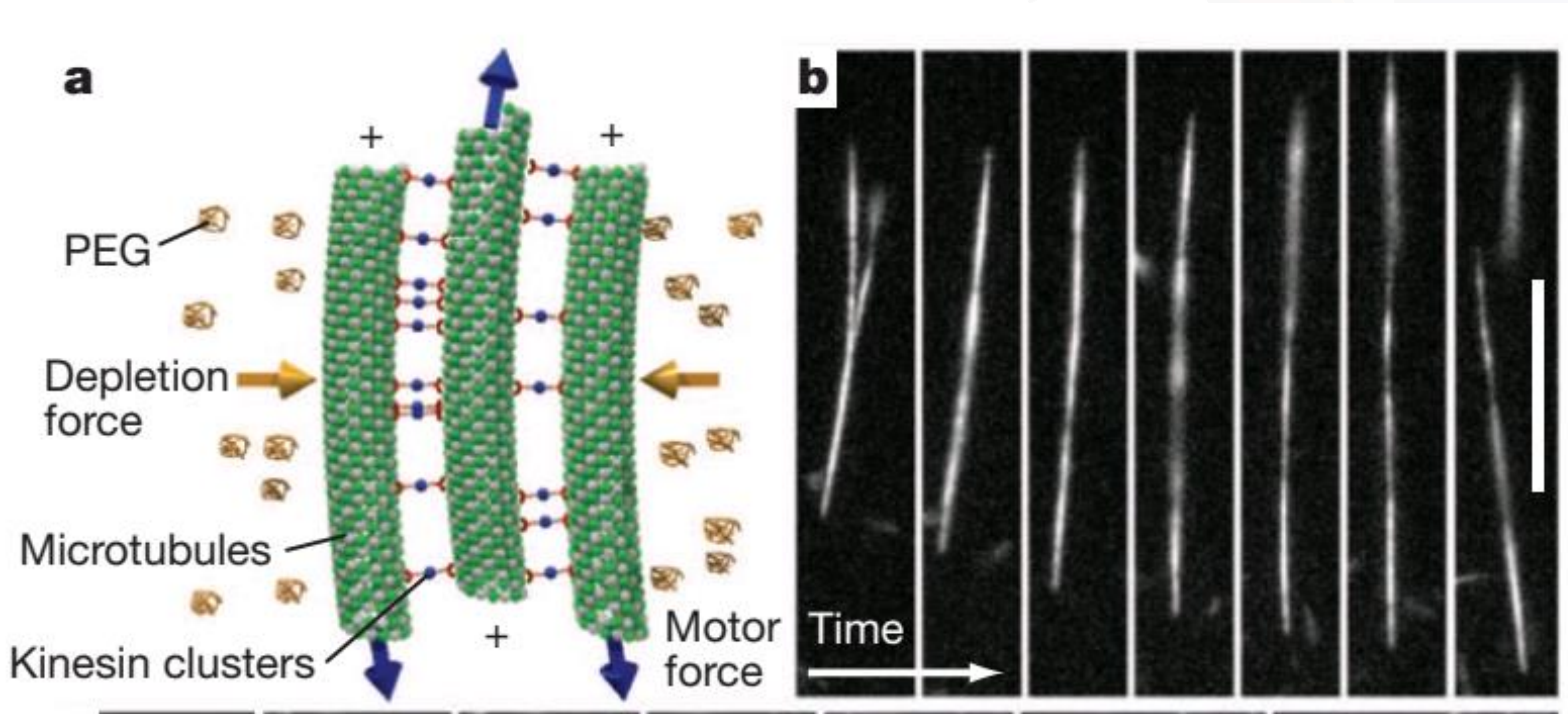
Topologically Active Materials

Materials that change their mechanical properties in time by alterations of their topology.



J. Palacci *et al., vol 339, Science 2013*

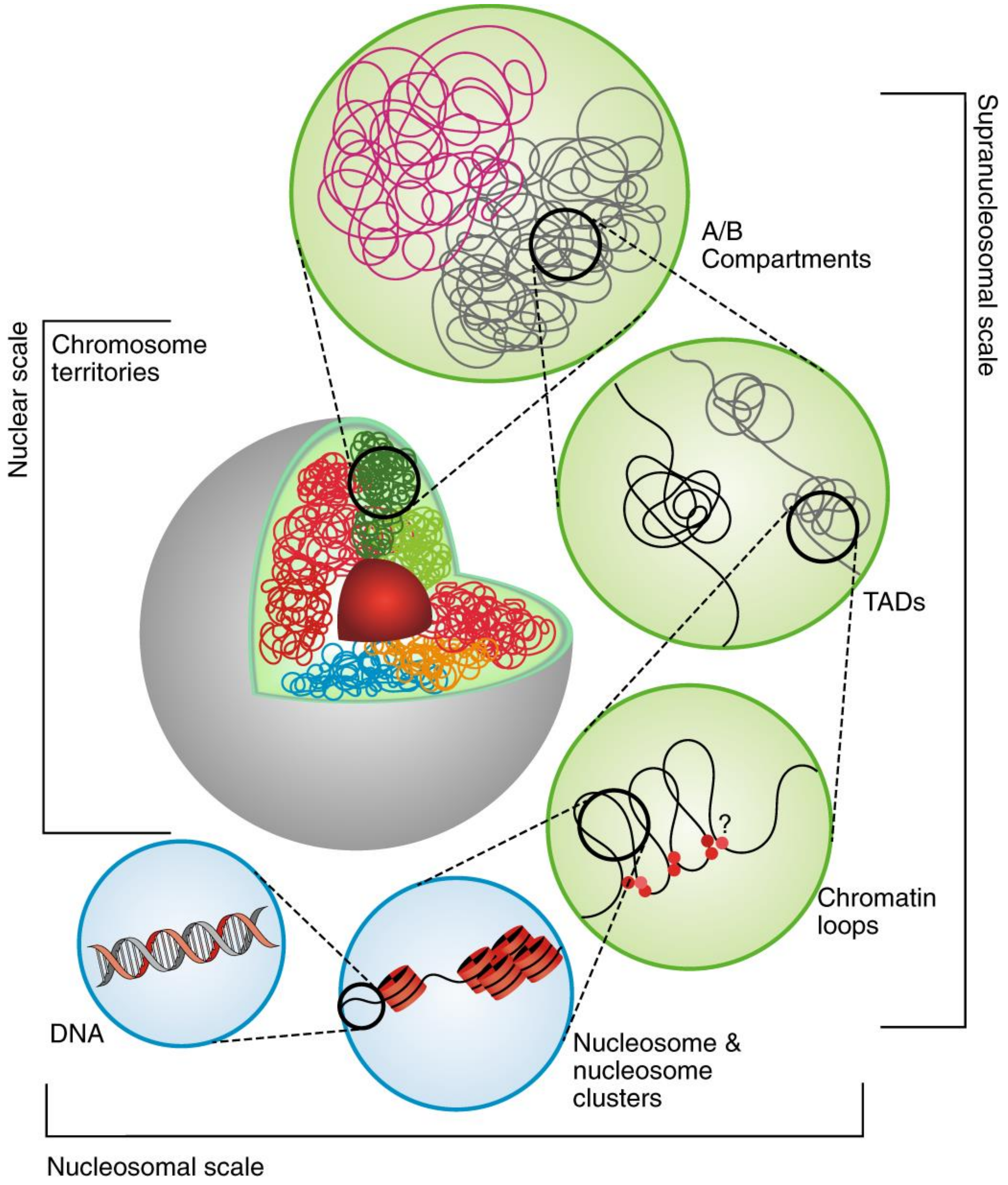


T. Sanchez *et al., vol 491, Nature 2012*

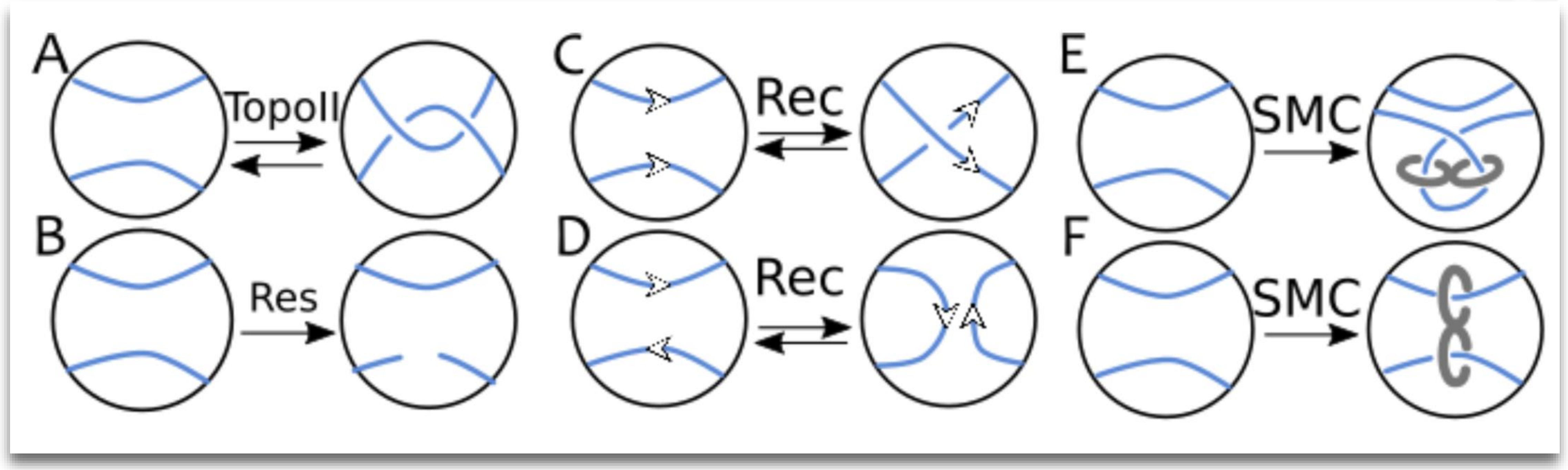
DNA manipulation in nature

Genome topology

genome topological manipulation by proteins such as Recombinase, SMCs, etc.



Nature's tools



Could these proteins be "used"
to make "topological" complex fluids?

Doğan, E.S., Liu, C. *Nature Plants* **4,** 521–529 (2018).

Topologically Active Biomaterials

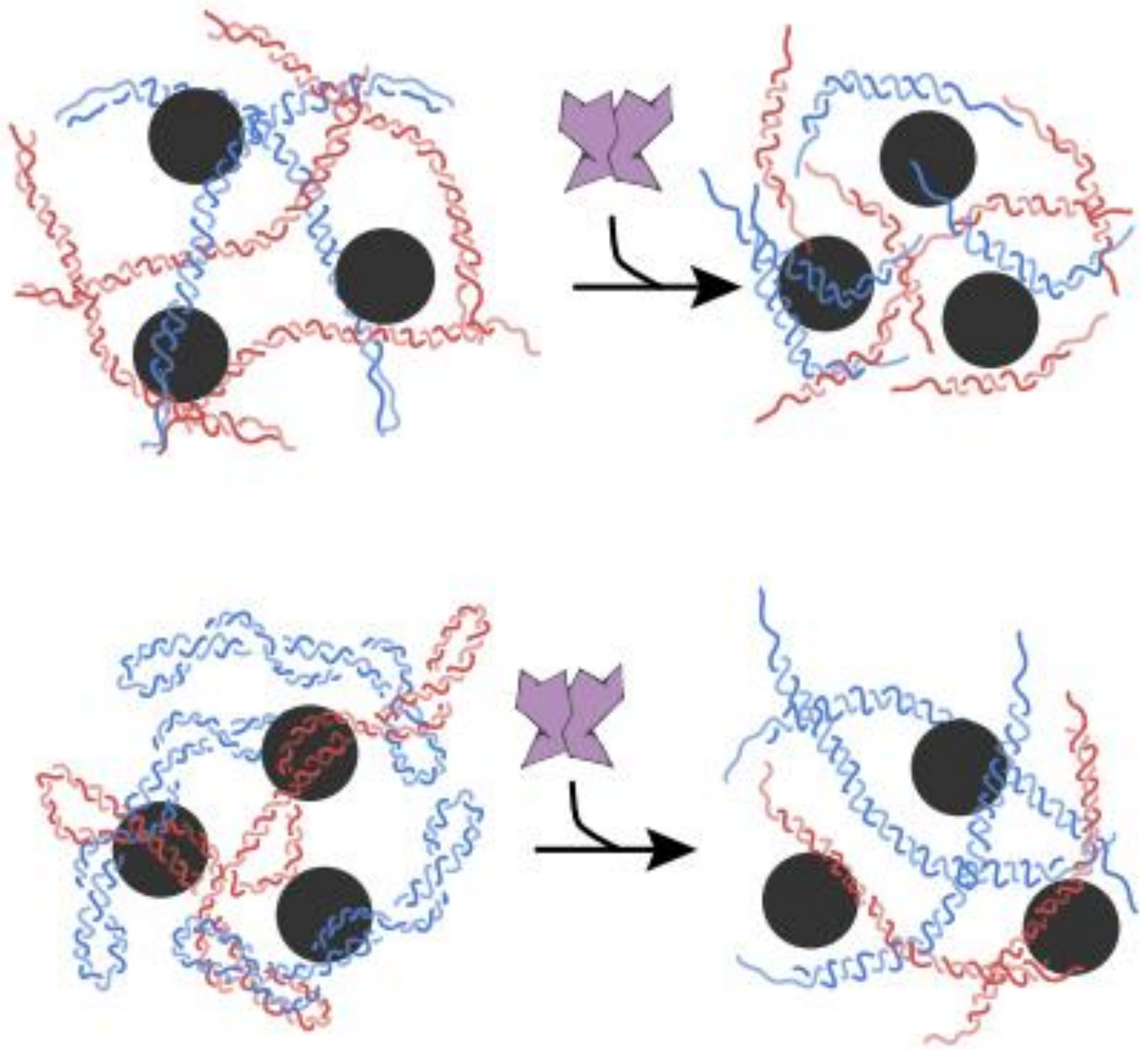
DNA biomaterials: what is the role of enzymes?

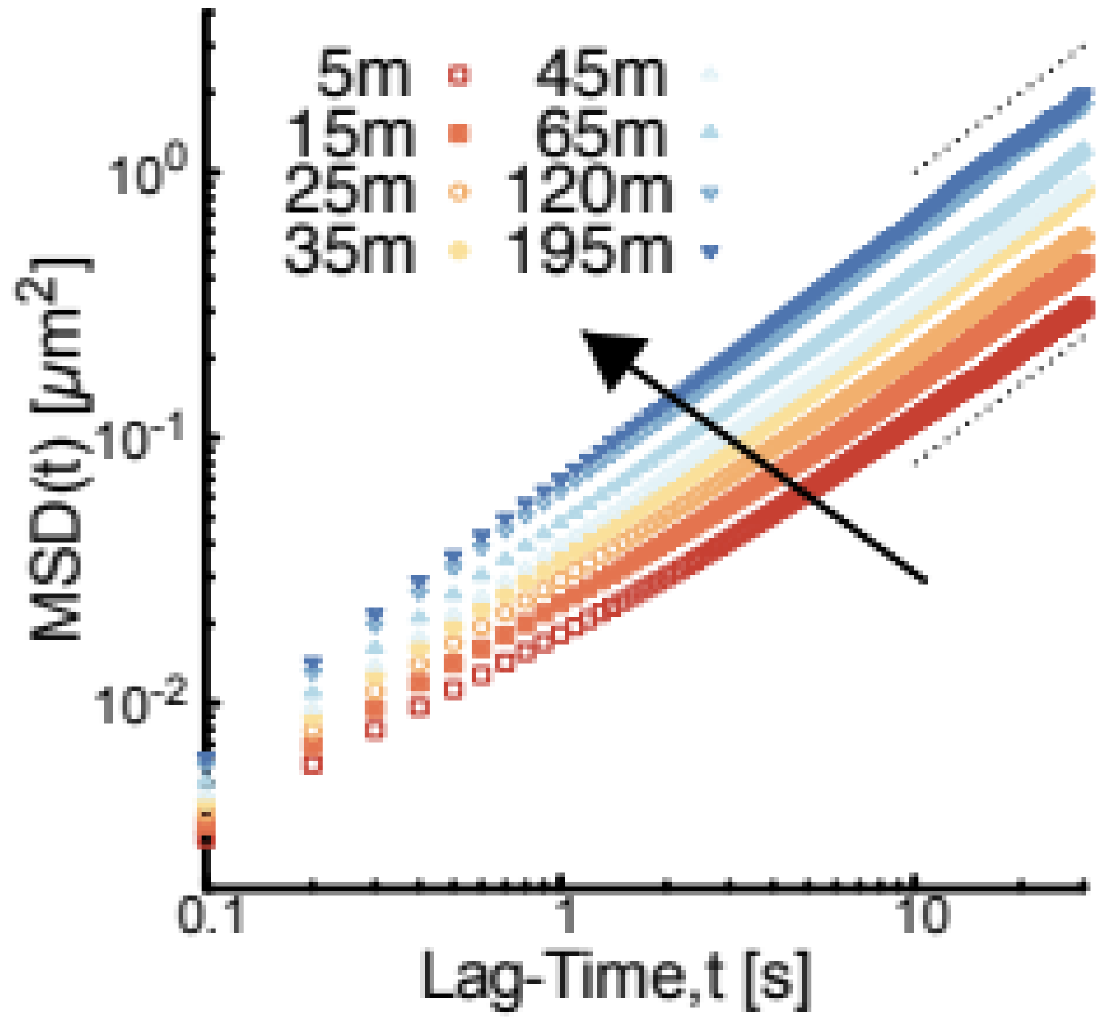
Micro-rheology

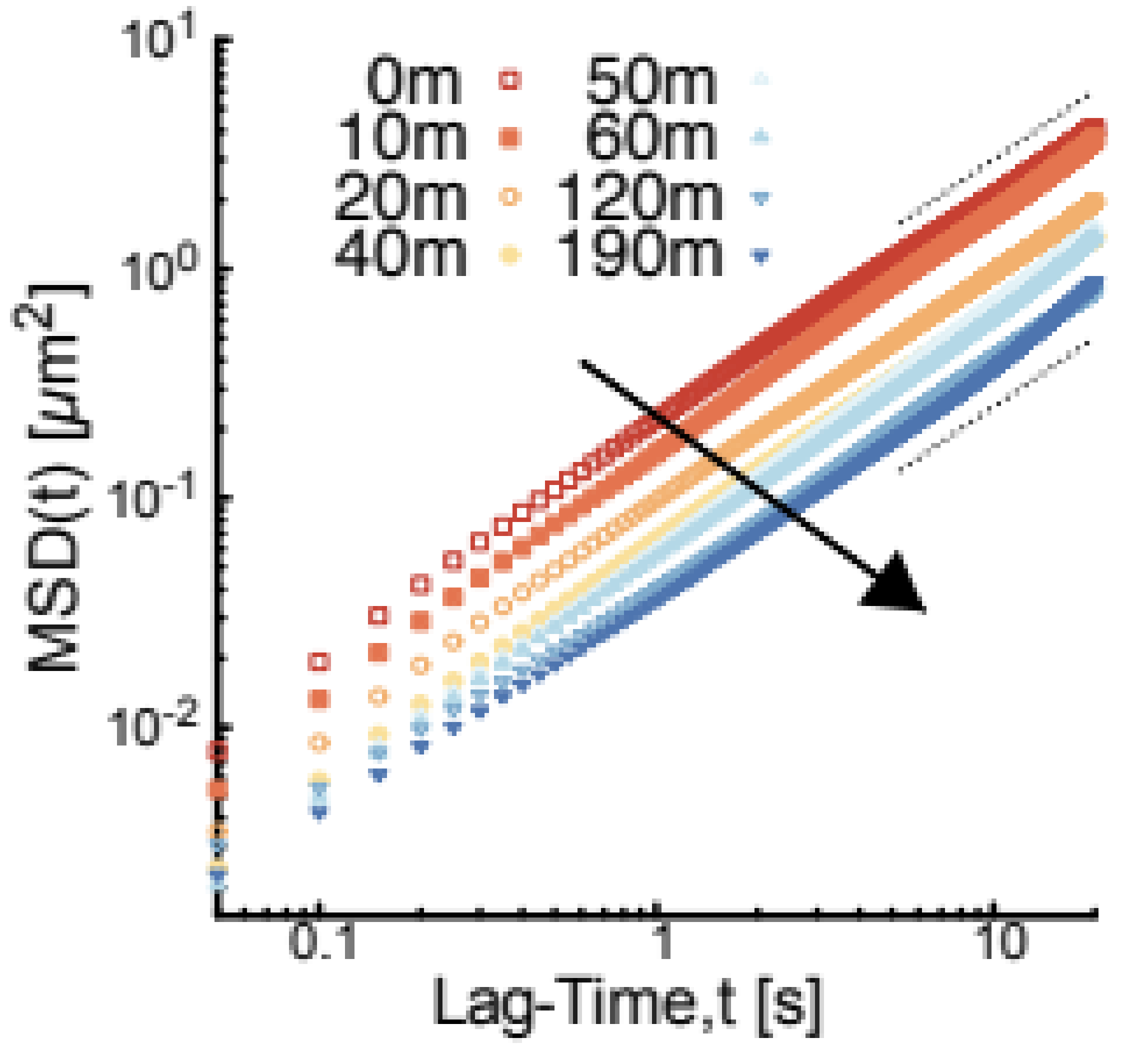
800 nm PVP-coated polystyrene beads

+

DNA solution





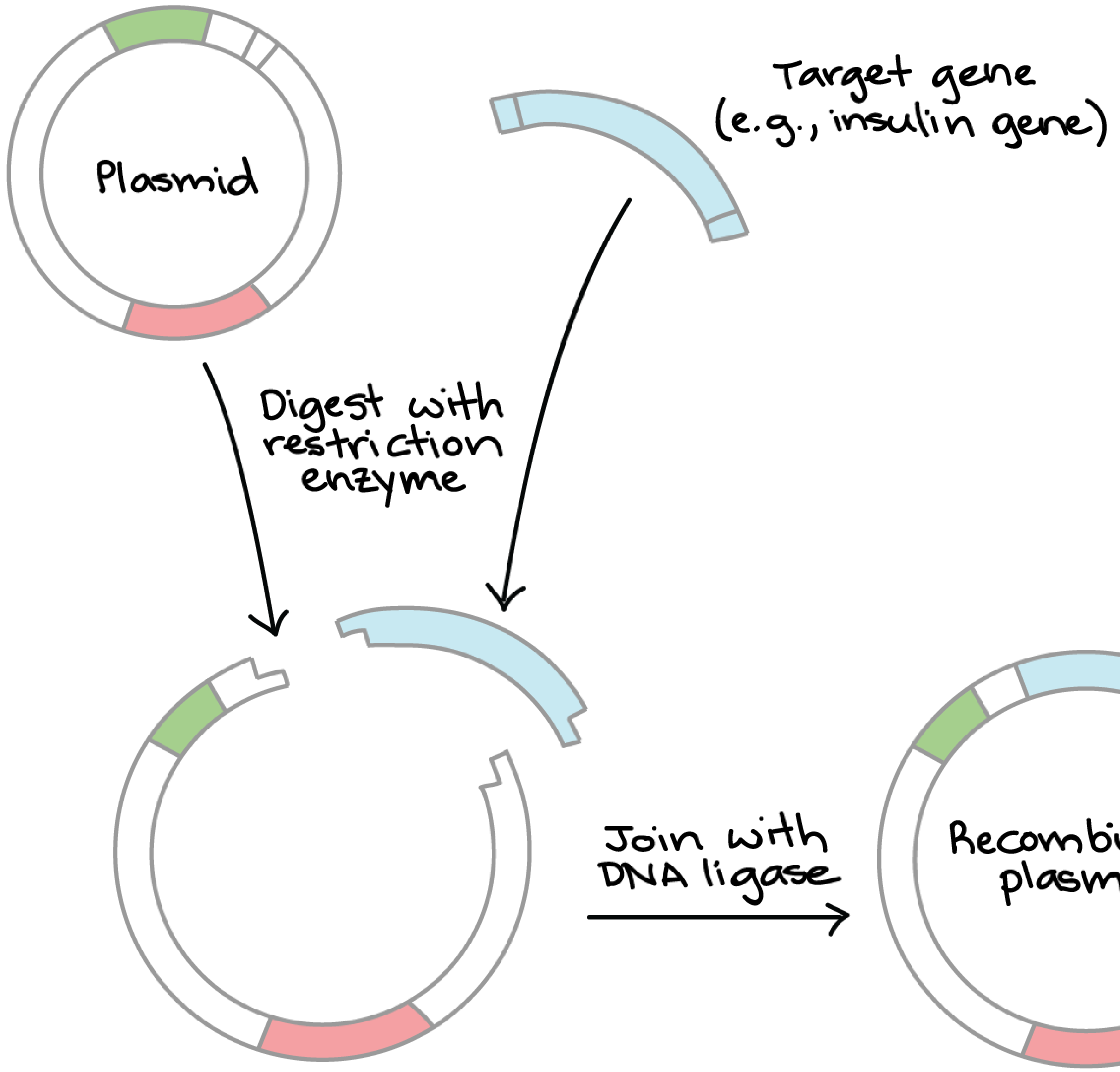


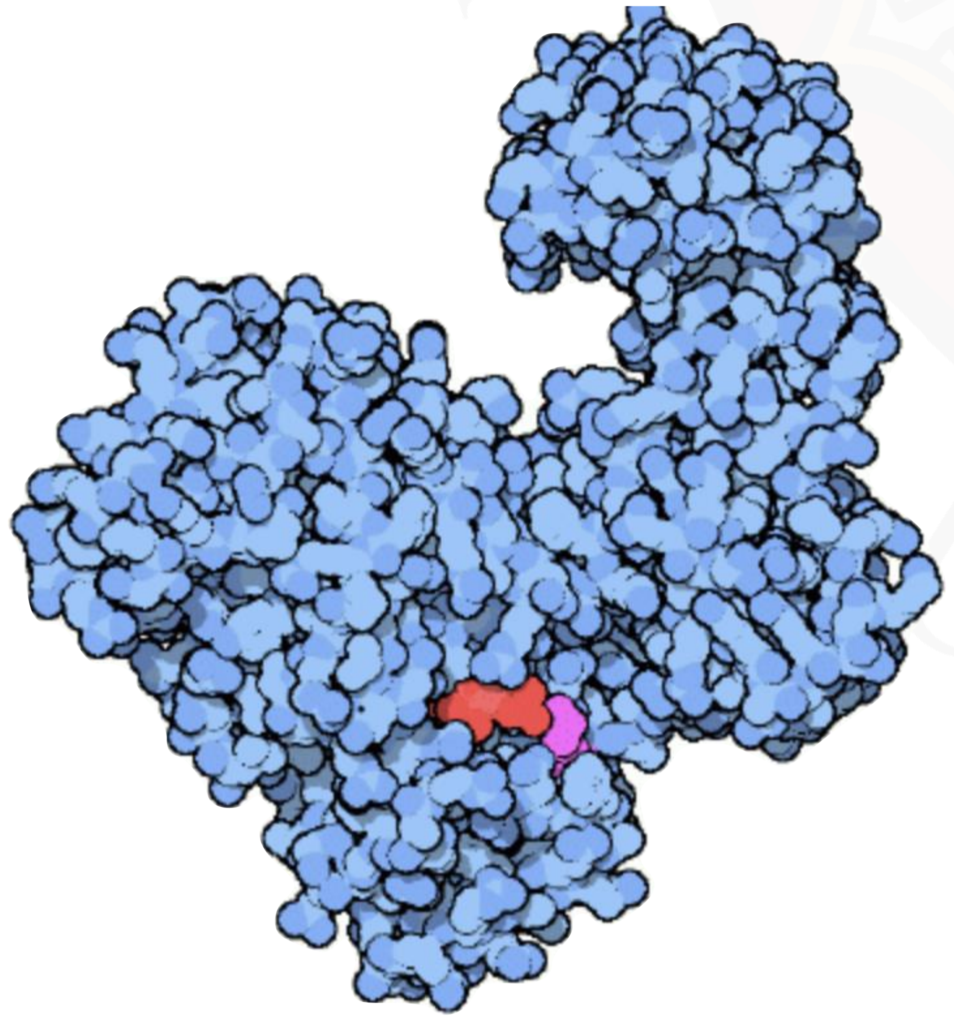
D. Michieletto *et al. Nat Commun* **13**, 4389 (2022)

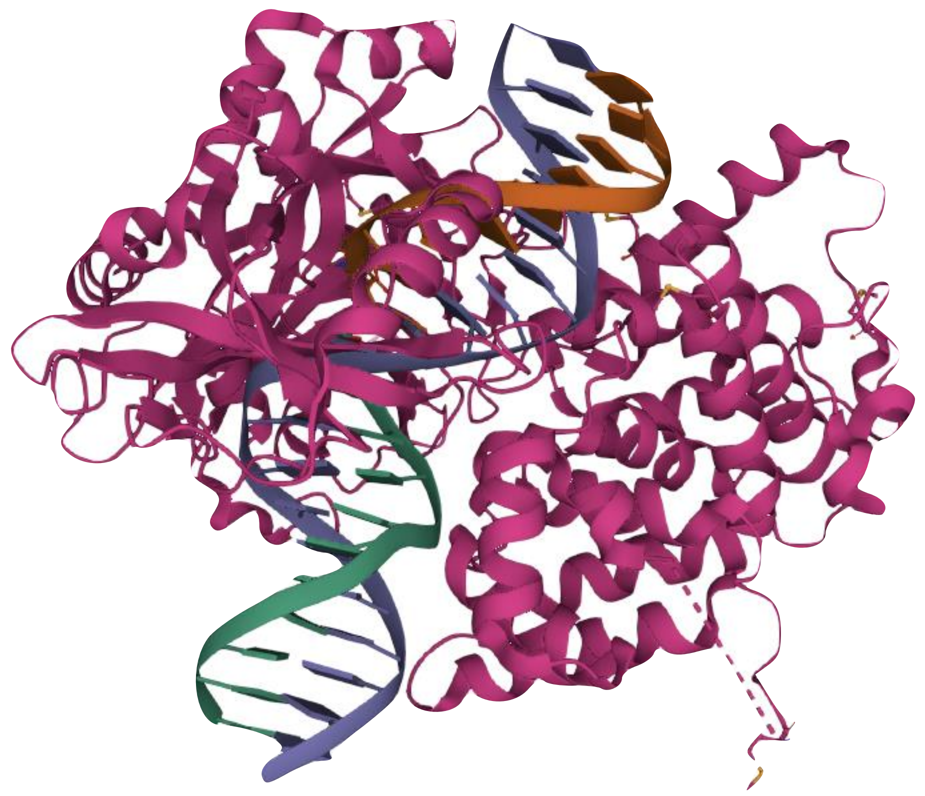
DNA Ligation

DNA ligase is a vital protein that consumes energy to link DNA fragments in vivo.

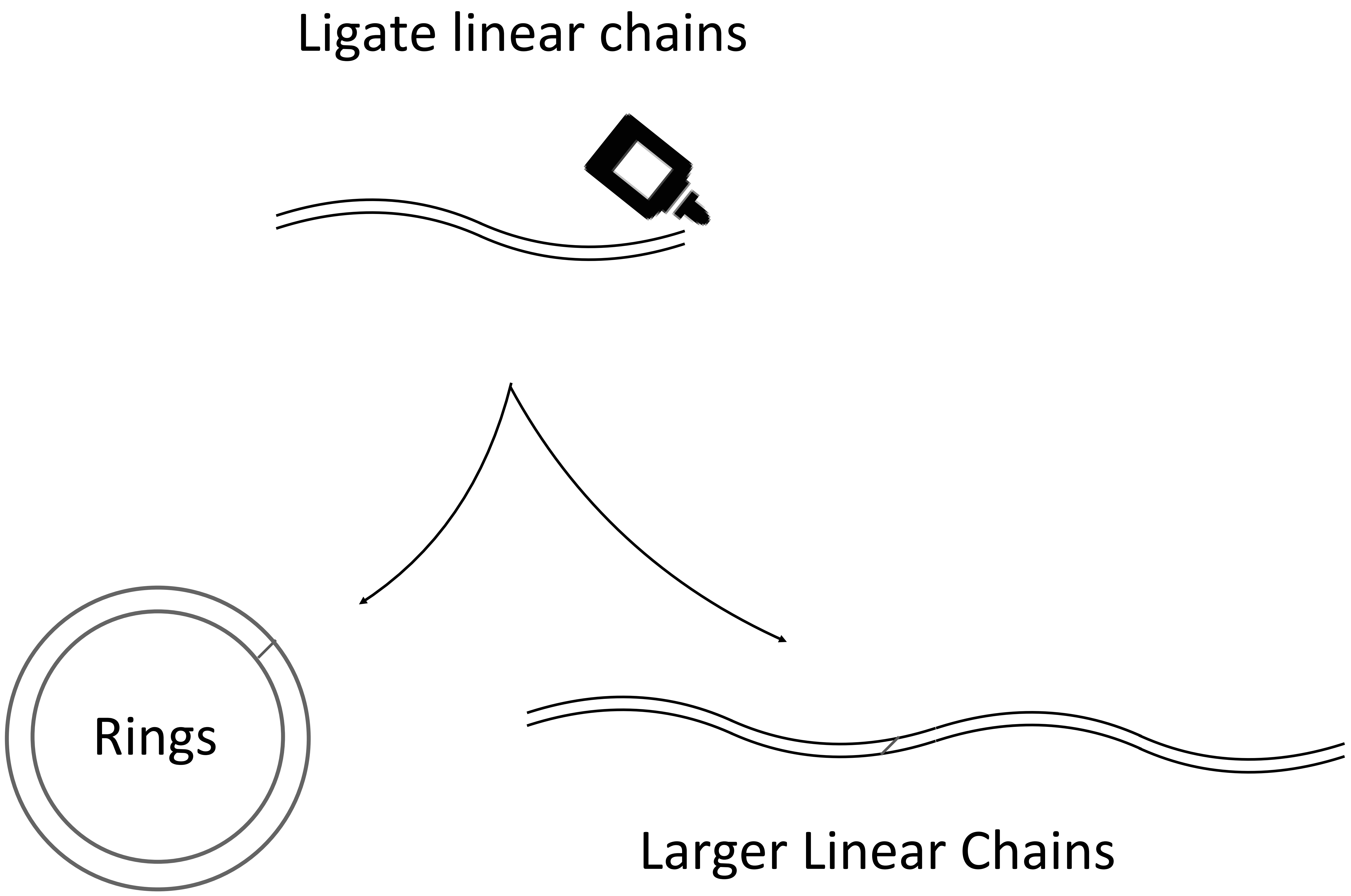
It is routinely used in the field of molecular biology to create recombinant genes



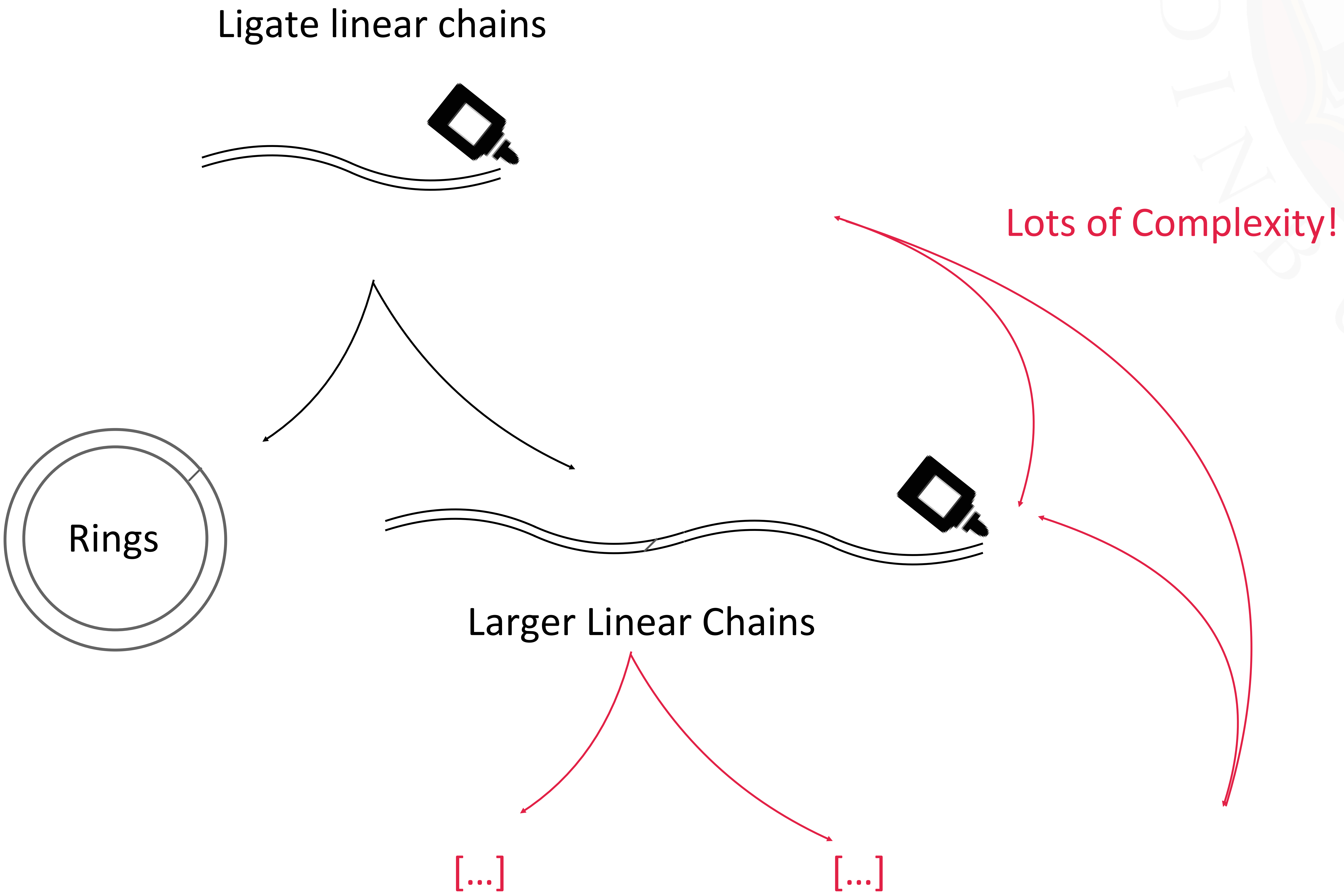




DNA Ligation



DNA Ligation



Polymer condensation

Smoluchowski equation - Mathematical Model of Ligase

$$\frac{dn_l}{dt} = \underbrace{\frac{1}{2}\sum_{i+j=l} n_i n_j k_1(i,j) - \sum_i n_i n_l k_1(i,l)}_{\text{Linear Chain Terms}} - \underbrace{n_l k_o(l)}_{\text{Ring Chain Term}}$$

$$< l > (t) = \frac{\sum_i n_i(t) l_i}{\sum_i n_i(t)}$$

In principle k_1, k_o depend on the polymer length

Solving the ODEs

Smoluchowski model

$$\frac{dn_l}{dt} = \frac{1}{2}\sum_{i+j=l} n_i n_j k_1(i,j) - \sum_i n_i n_l k_1(i,l) - n_l k_o(l)$$

De Gennes: $\kappa_1\left(\frac{1}{{l_o}_i^{\alpha}} + \frac{1}{{l_o}_j^{\alpha}}\right)\left({l_o}_i^{\nu} + {l_o}_j^{\nu}\right)$

$$\kappa_o\left(\frac{1}{{l_o}_i^{3\nu}}\right)$$

Rate of ring to linear chains formation

$$\kappa = \frac{2\kappa_o}{n_o \kappa_1}$$

where n_o is the number density of monomeric chains with length l_o

$\kappa > 1$ Ring chains dominated regime

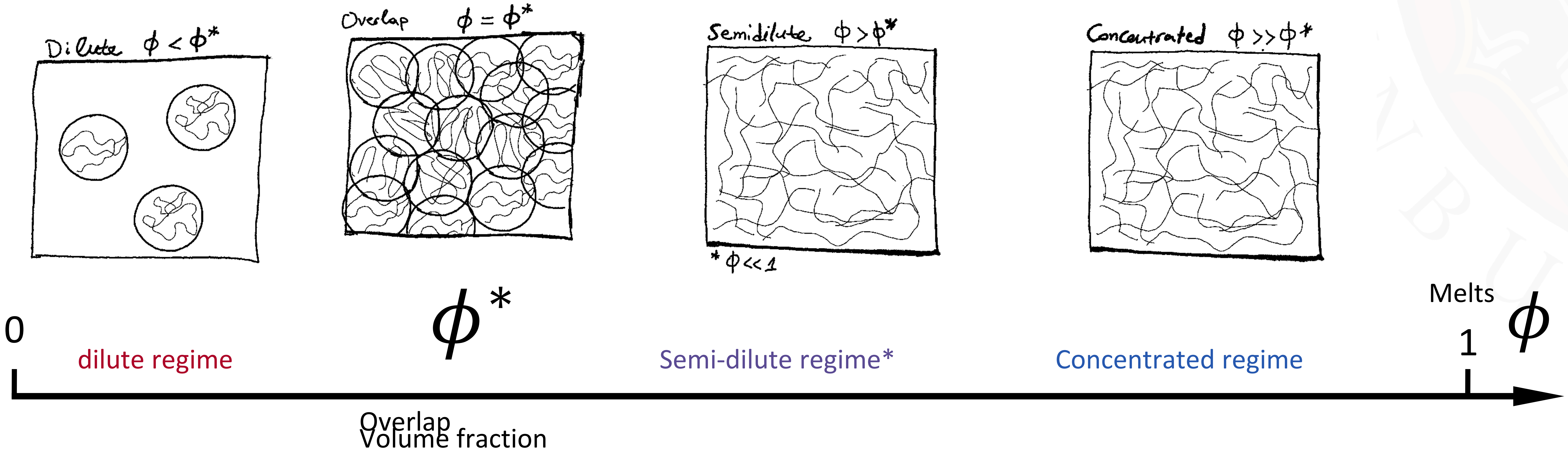
$\kappa = 1$ Equal amount of ring and linear chains

$\kappa < 1$ Linear chains dominated regime

P. De Gennes, 76(6):3316-3321 JCP (1982),

P. De Gennes, 76(6):3322–3326 JCP (1982)

Polymer physics



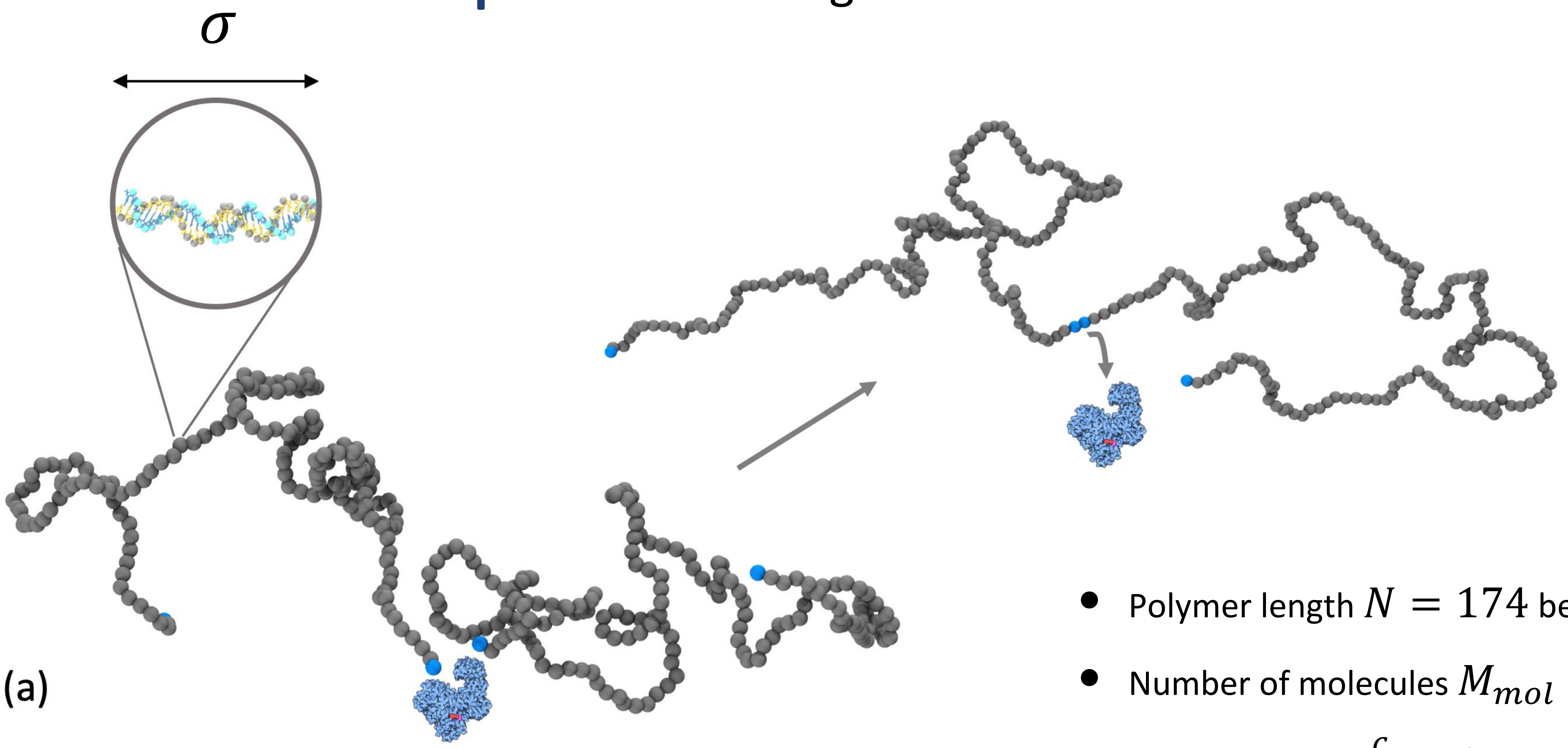
$$\phi^* = c^* v_{mon} \qquad c^* = \frac{3N}{4\pi R_g^3}$$

*This regime does not exist for all polymers, usually seen at low molecular weight polymers.

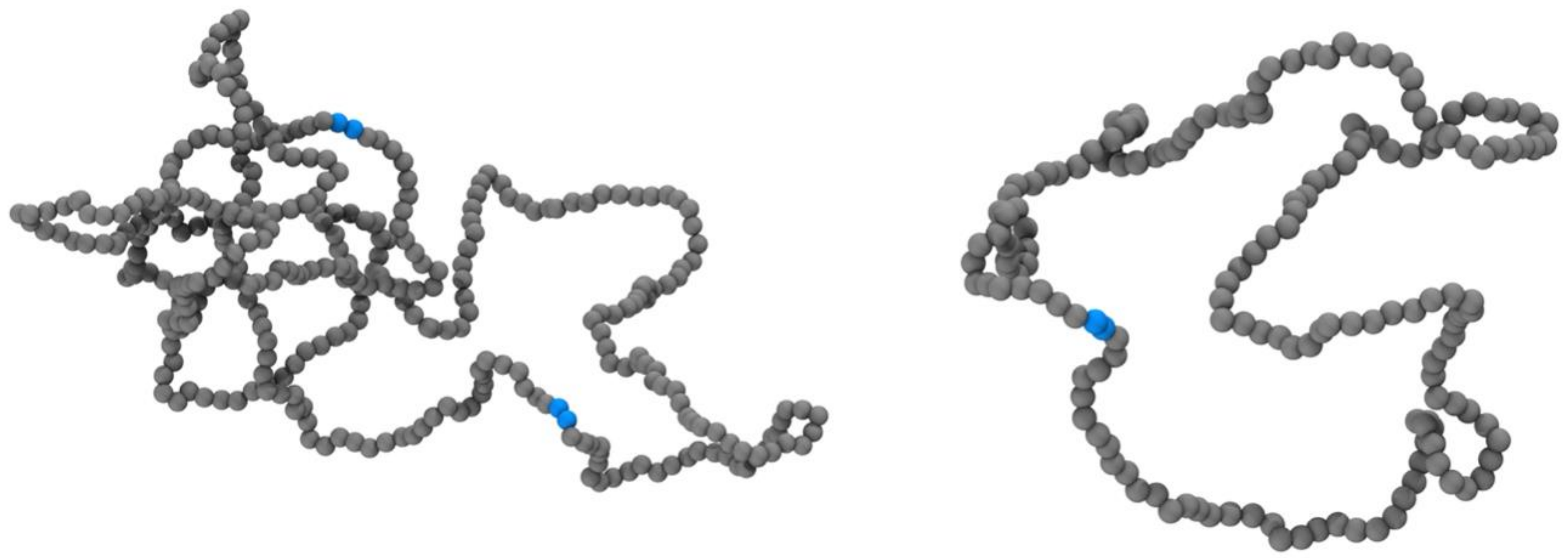
Rubinstein, M. and Colby, R. H. (2003) Polymer physics.

Simulation set up

Ligase in simulations



(a)

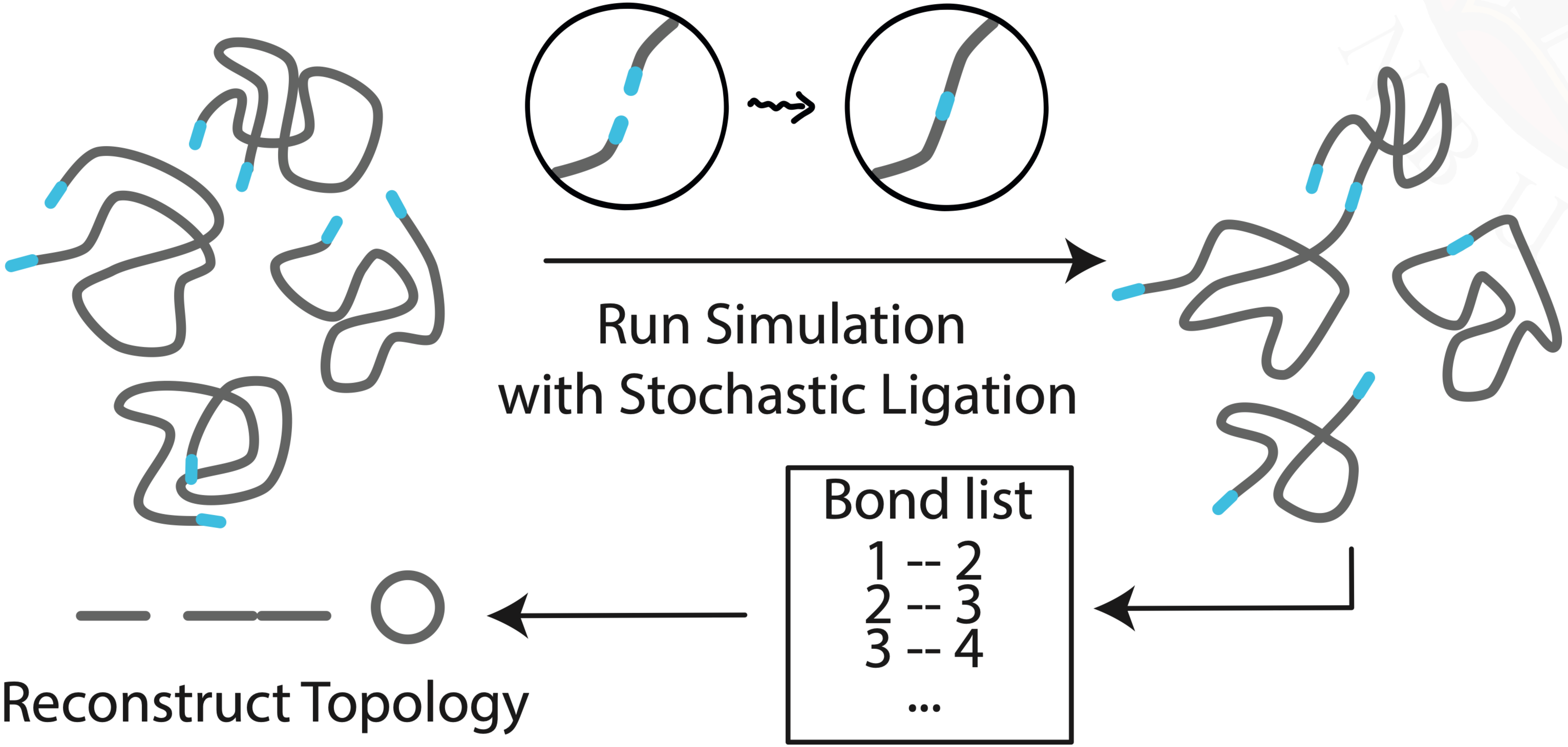


(b)

- Polymer length $N = 174$ beads, $\sigma = 38bp$
- Number of molecules $M_{mol} = 200$
- Concentrations $\frac{c}{c^*} = \{0.01, \dots, 1\}$
- Relaxation time τ_B dependent on concentration
- Ligation rate /
  rate with which ligase is recruited $= 10^{-1}\tau_B^{-1}$
  equivalently: every 100 steps a ligation
  is attempted with probability of success 0.1

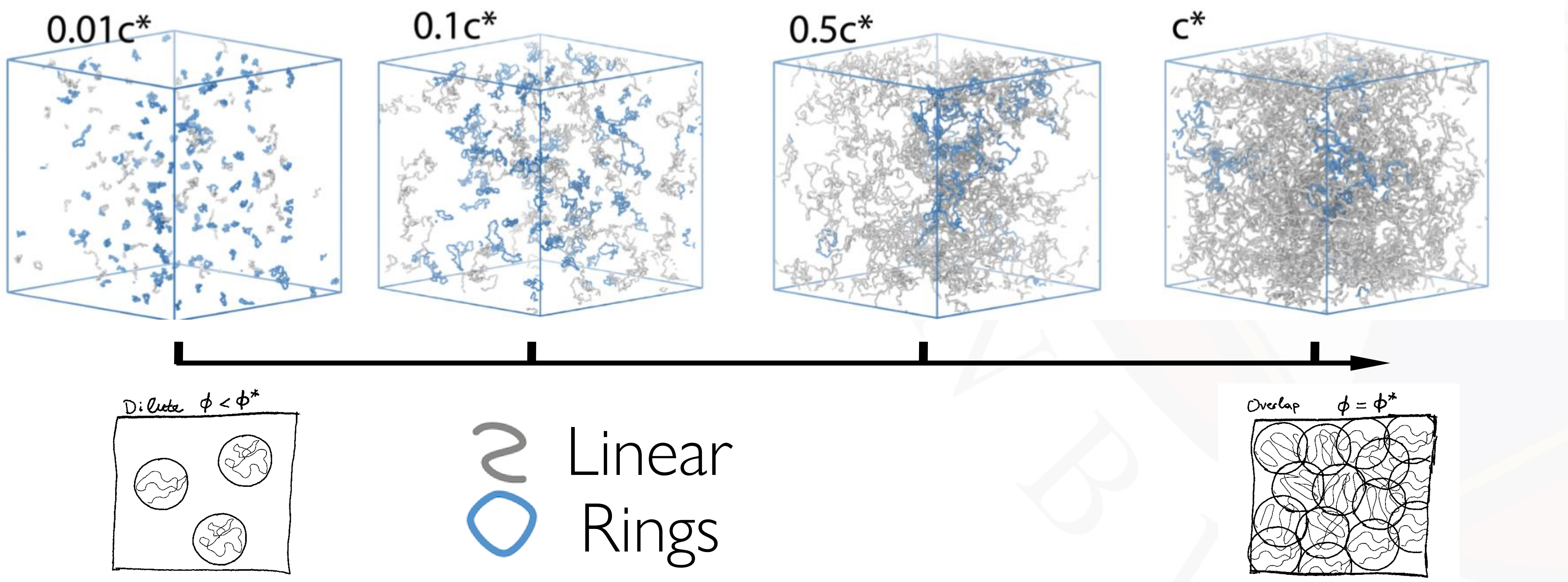
Topology reconstruction

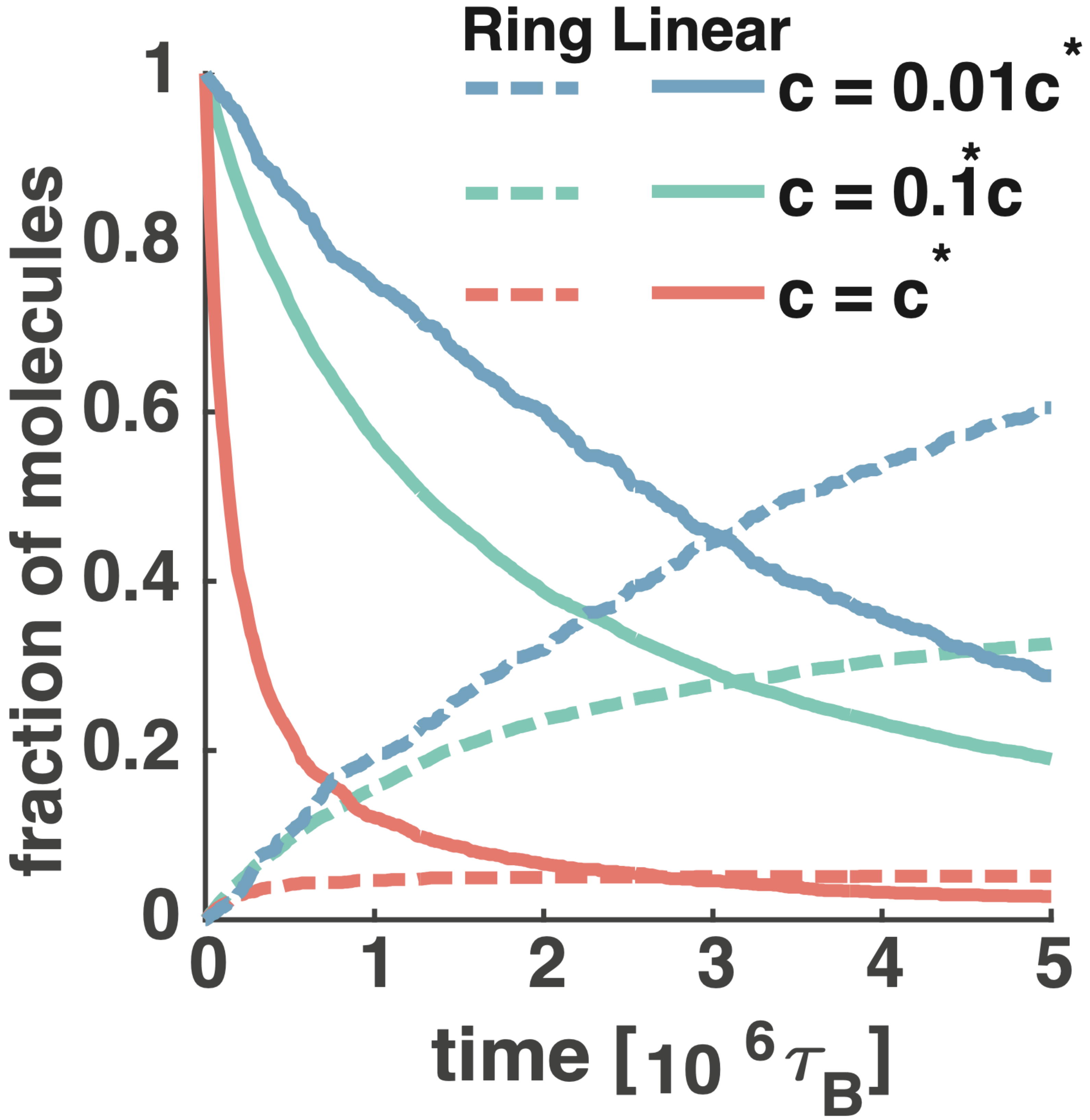
For GitHub repository

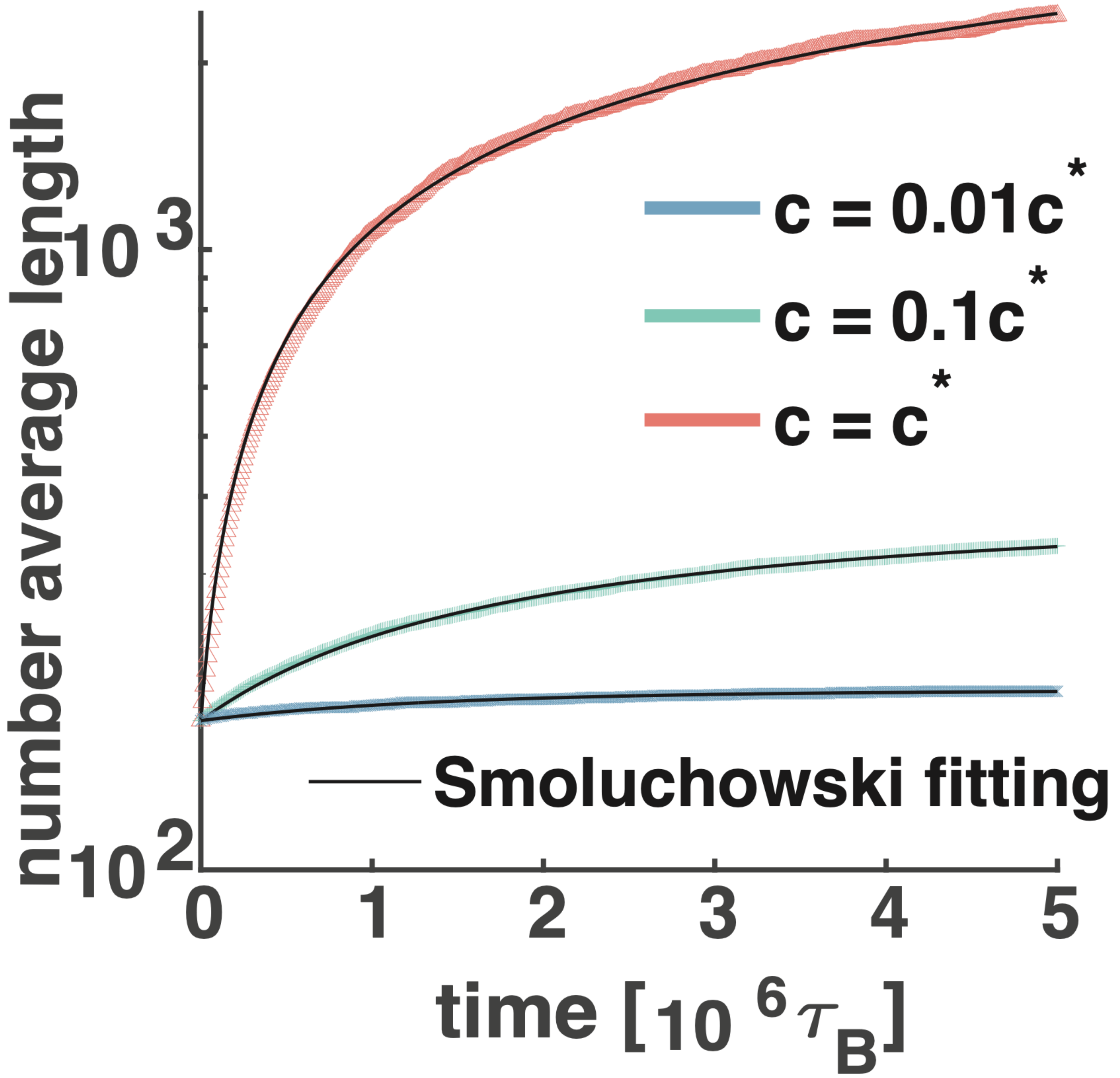


Towards the overlapping concentration

Microstructure as $c \to c^*$



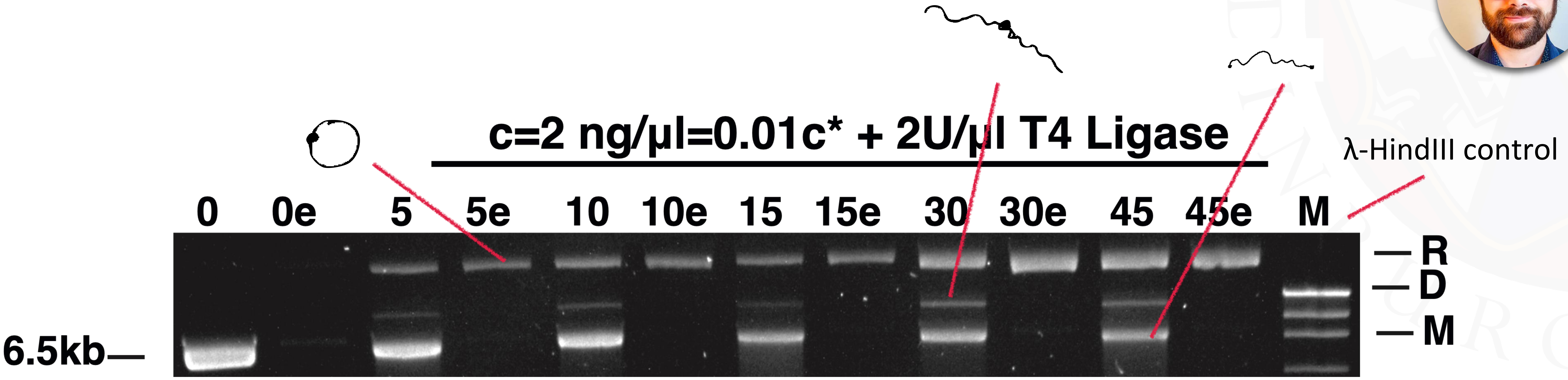




$$c^* = \frac{3N}{4\pi R_g^3}$$

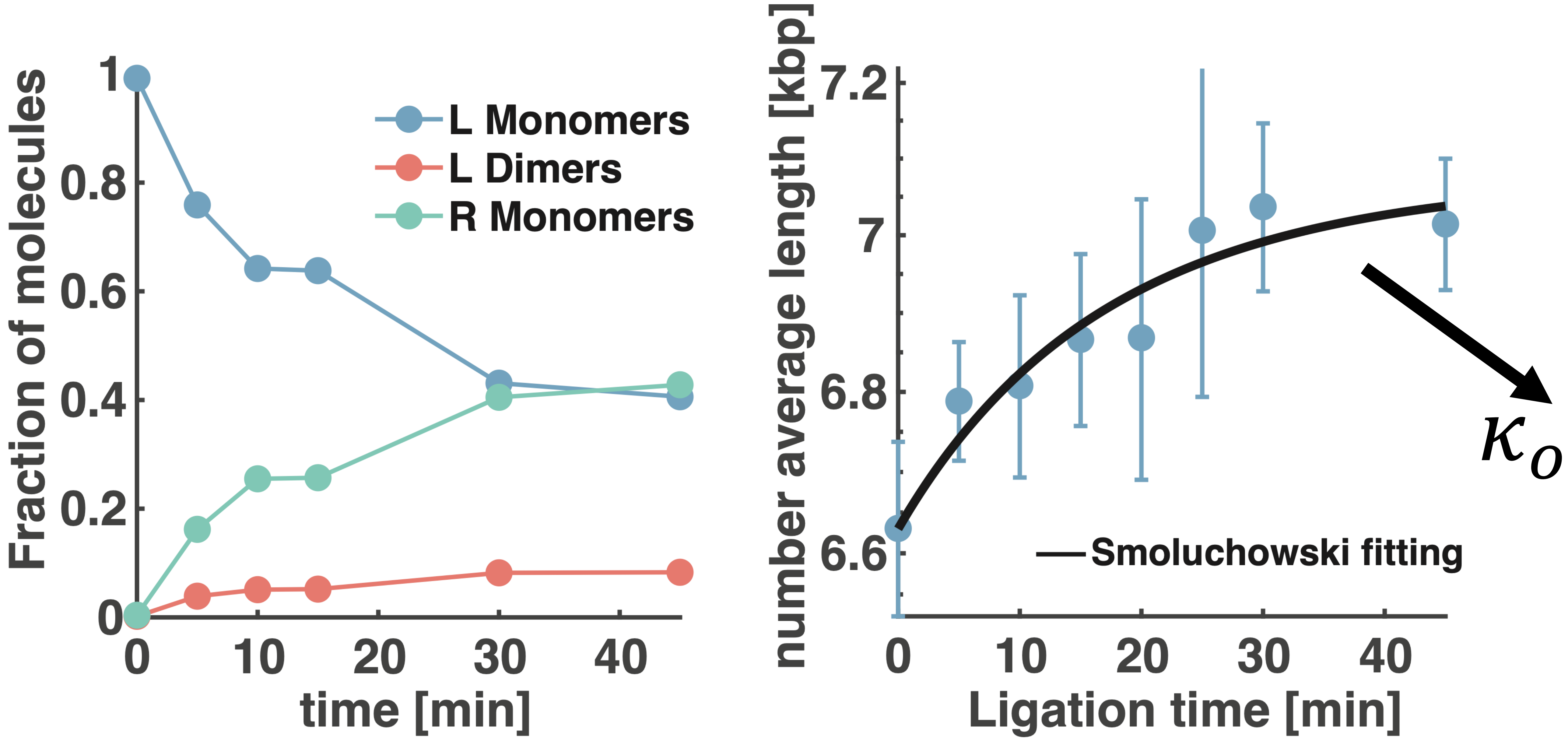
κ_o and κ_1

Gel Electrophoresis on 1288 plasmid



Linear changes can be digested by exonuclease

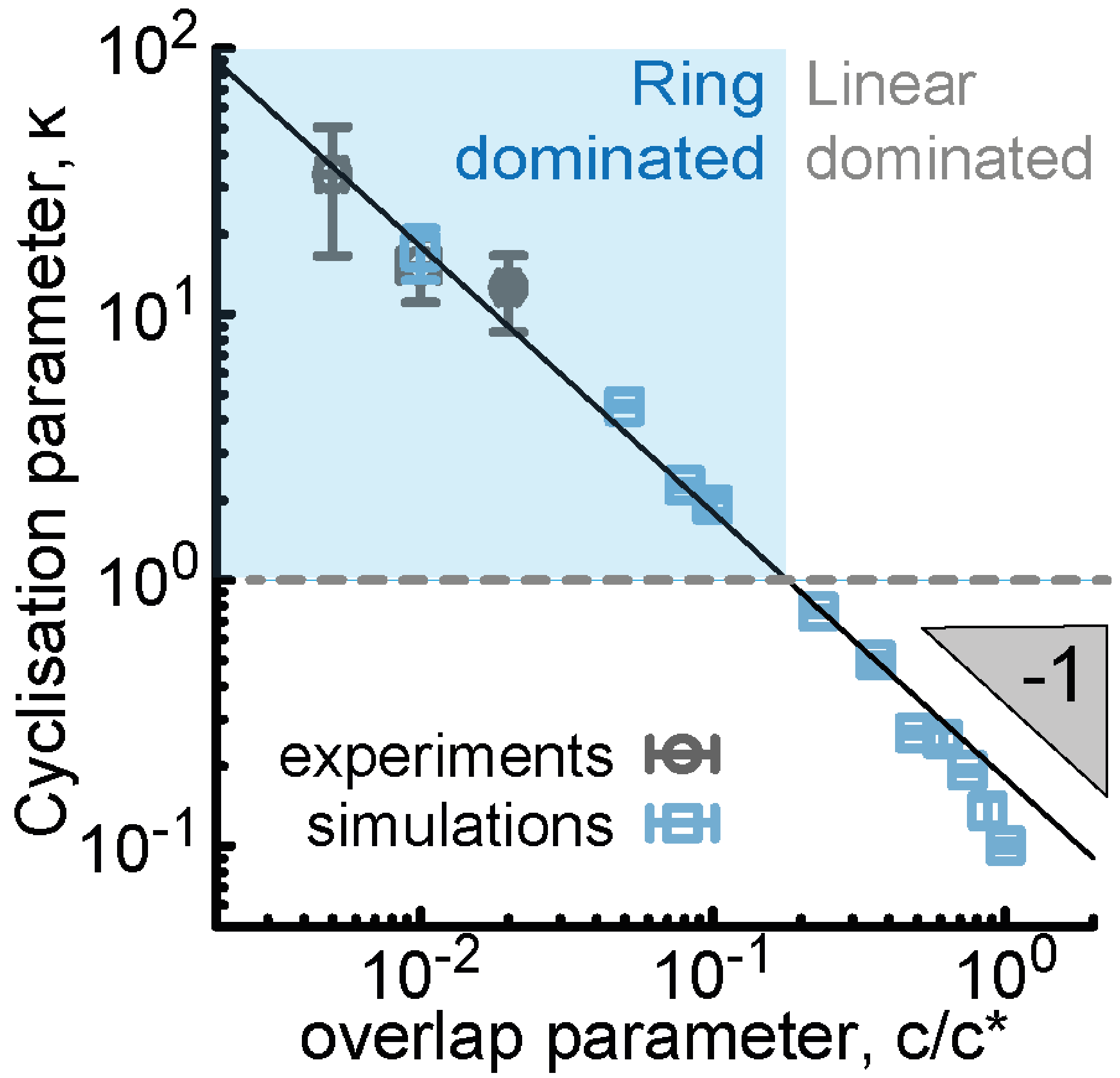
Removing them from the solution, thus differentiating bands of linear or ring DNA



κ_o and κ_1

Runaway transition point

Runaway := the regime at which at least one chain permanently escapes cyclisation



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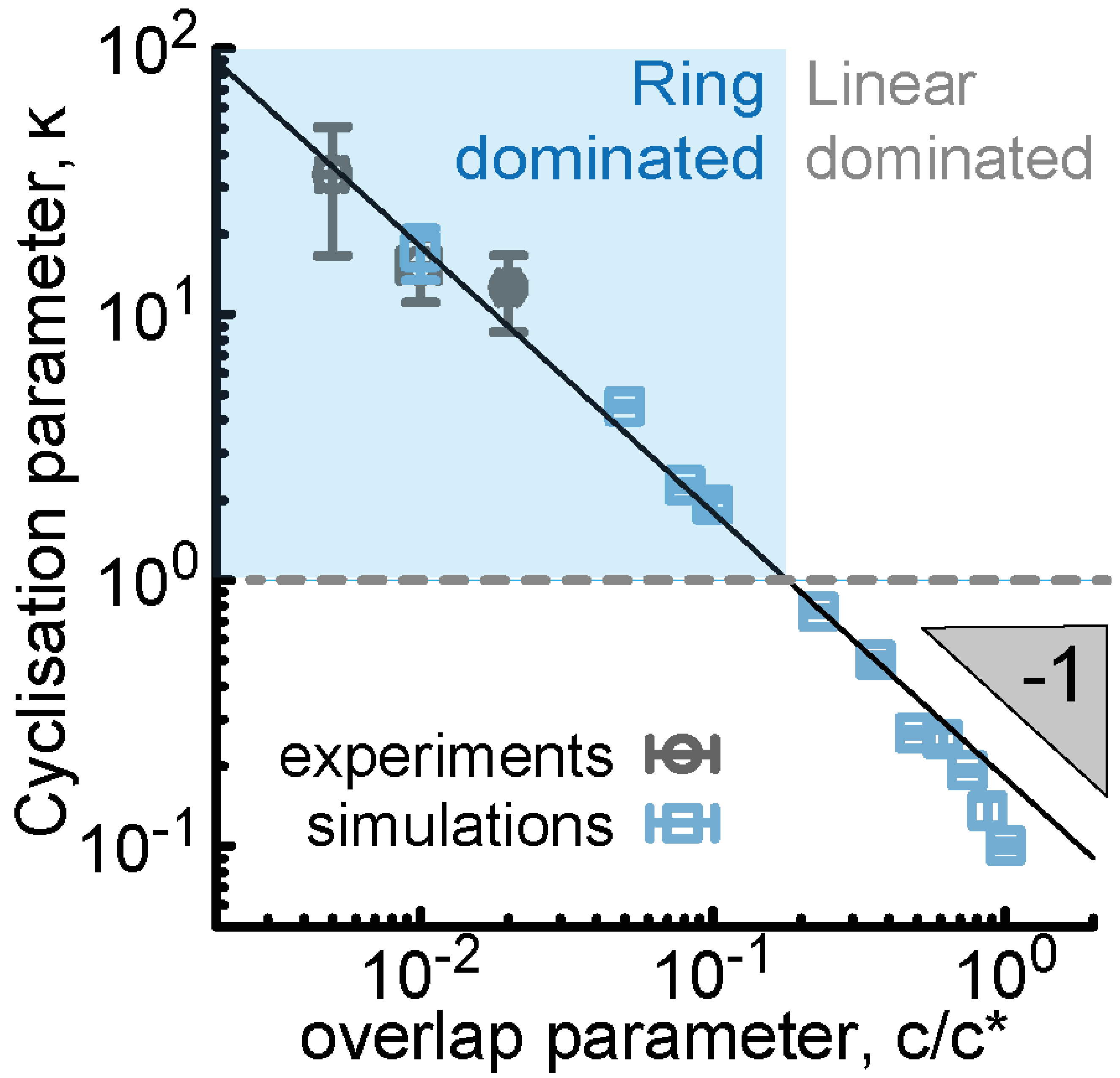
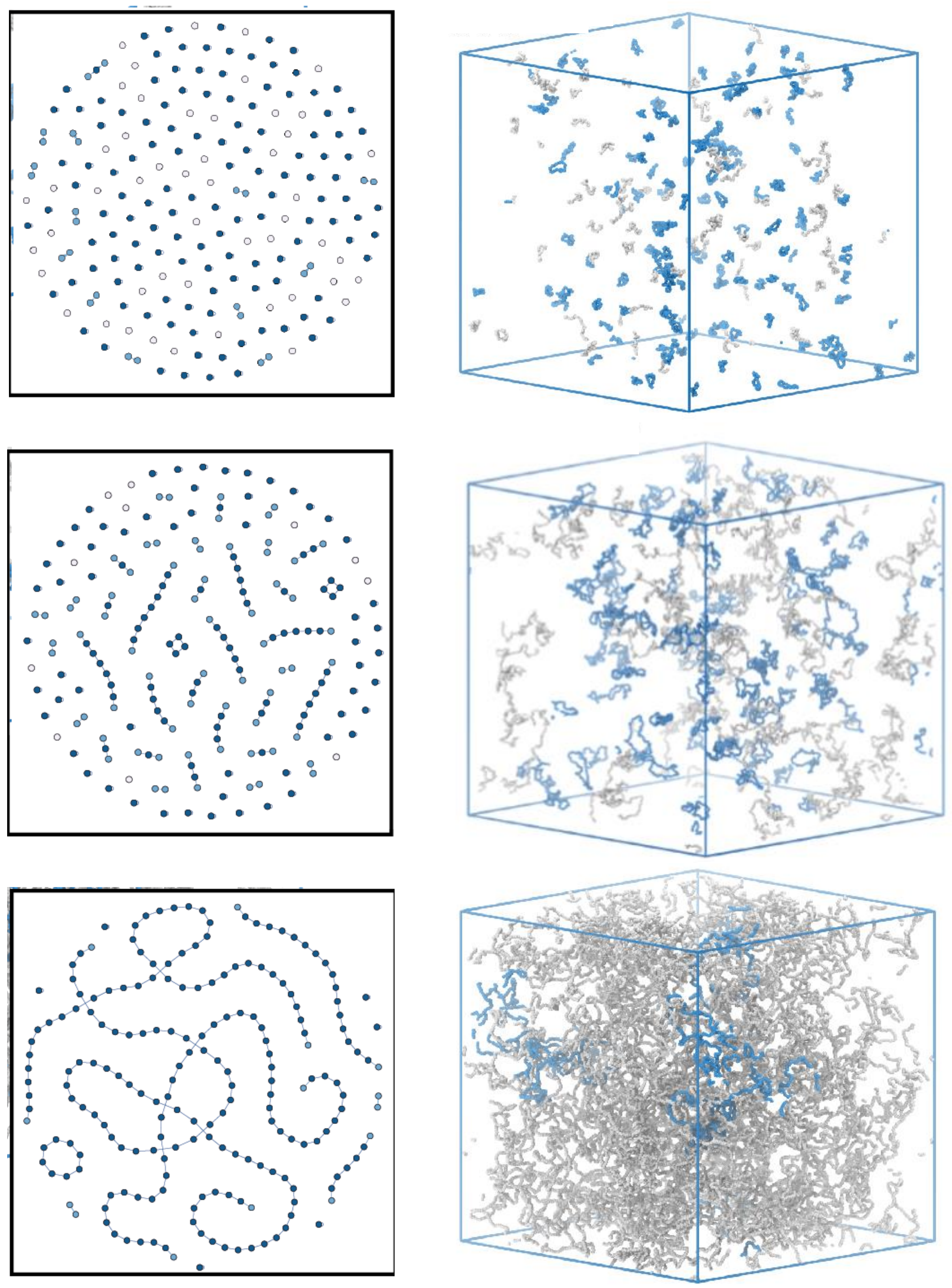


Concentration | Network | Simulation box

$c^* = 0.01c$

$c^* = 0.1c$

$c^* = c$



Grey = no connection
Light blue = 1 connection
Dark blue = 2 connections

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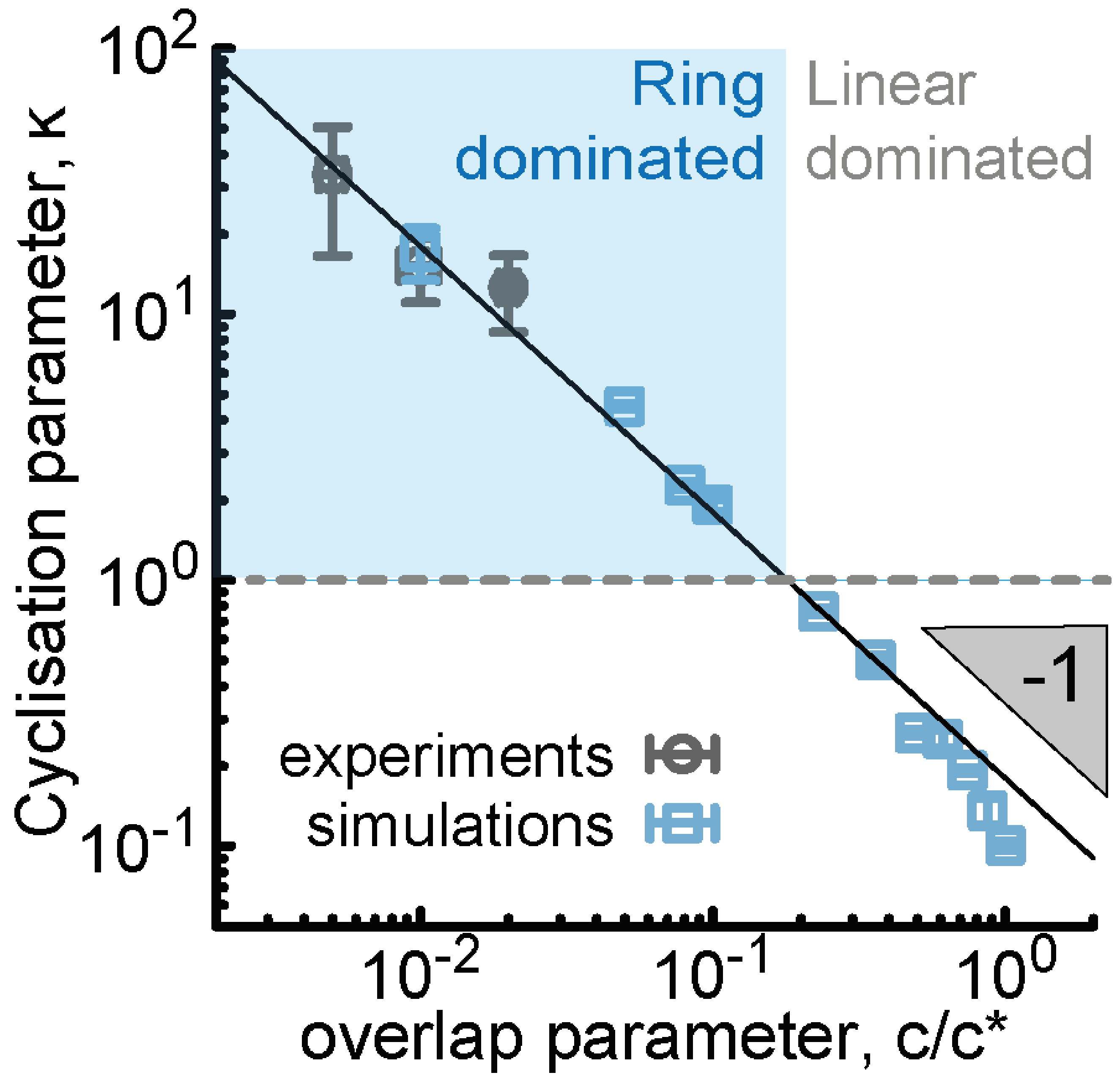

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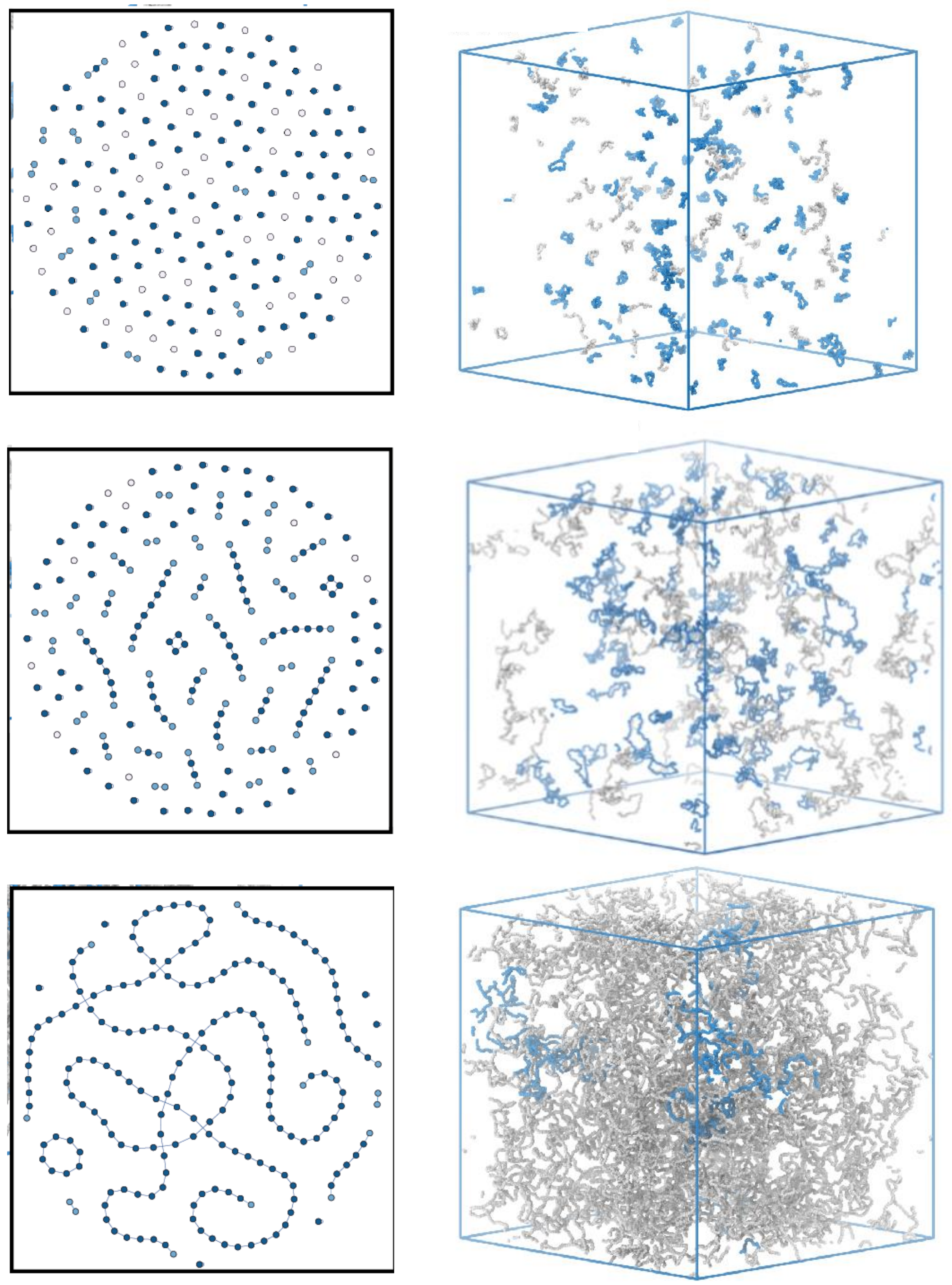
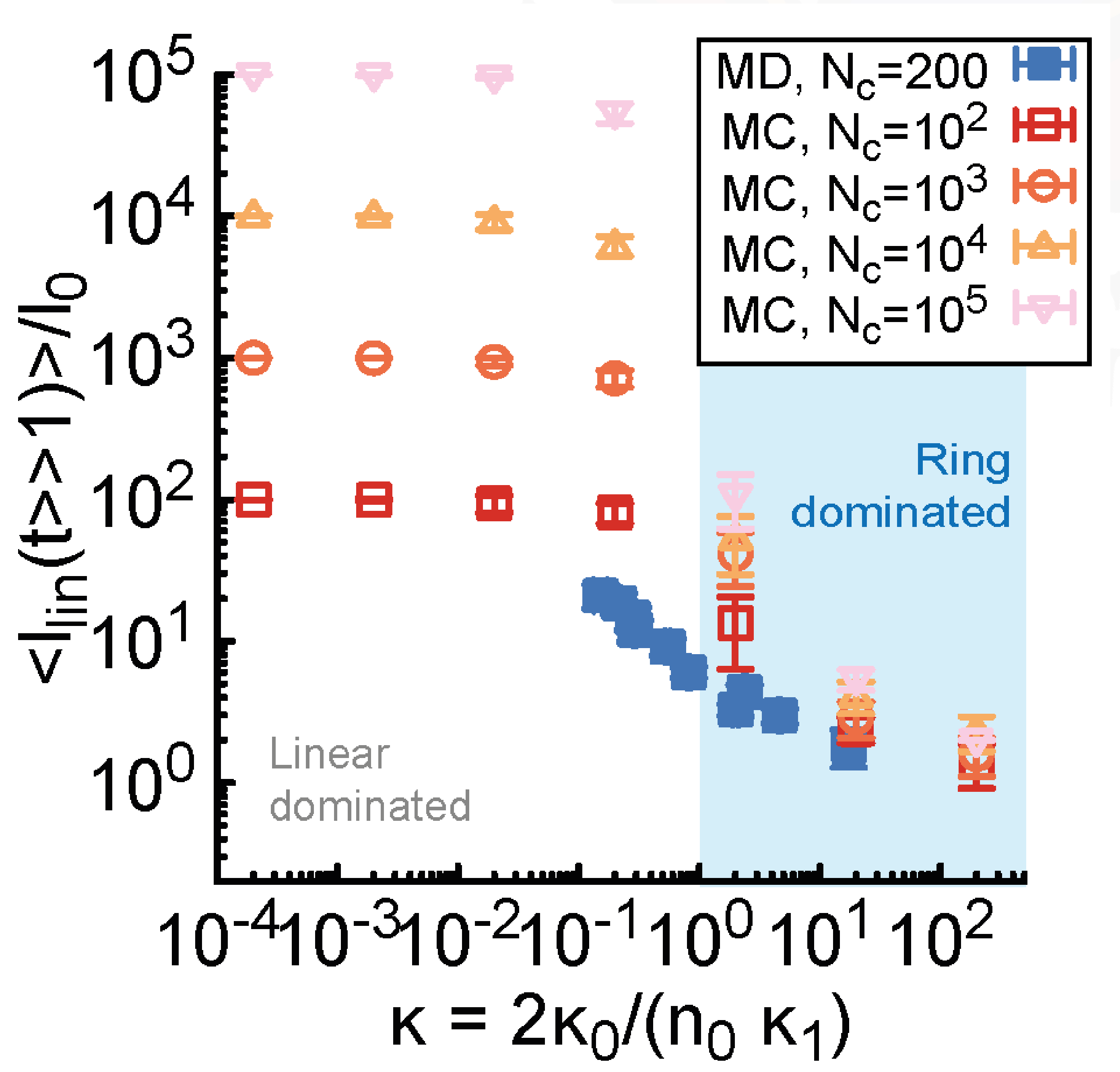
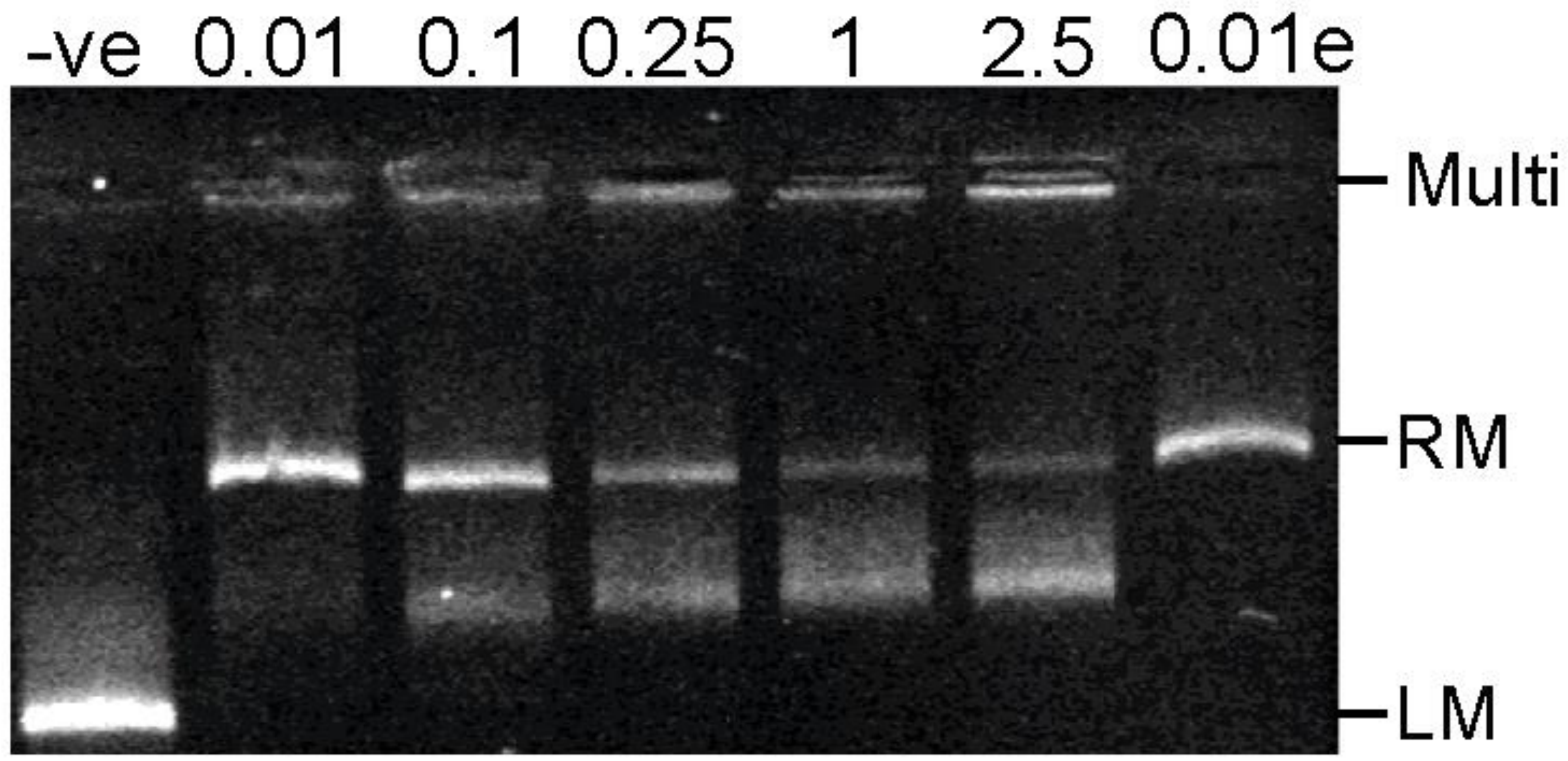




Micro-rheology

c/c^*

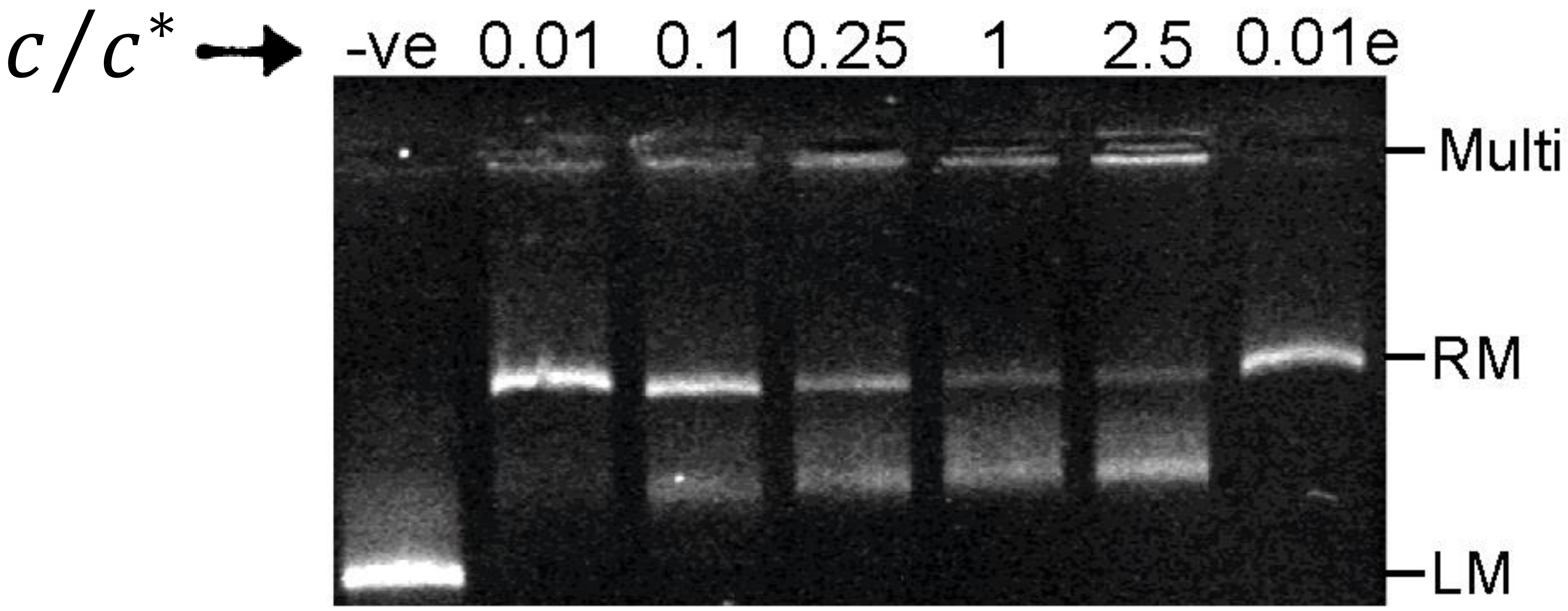


LM = Linear Monomers

RM = Ring Monomers

Multi = various lengths of high M_w structures

Micro-rheology



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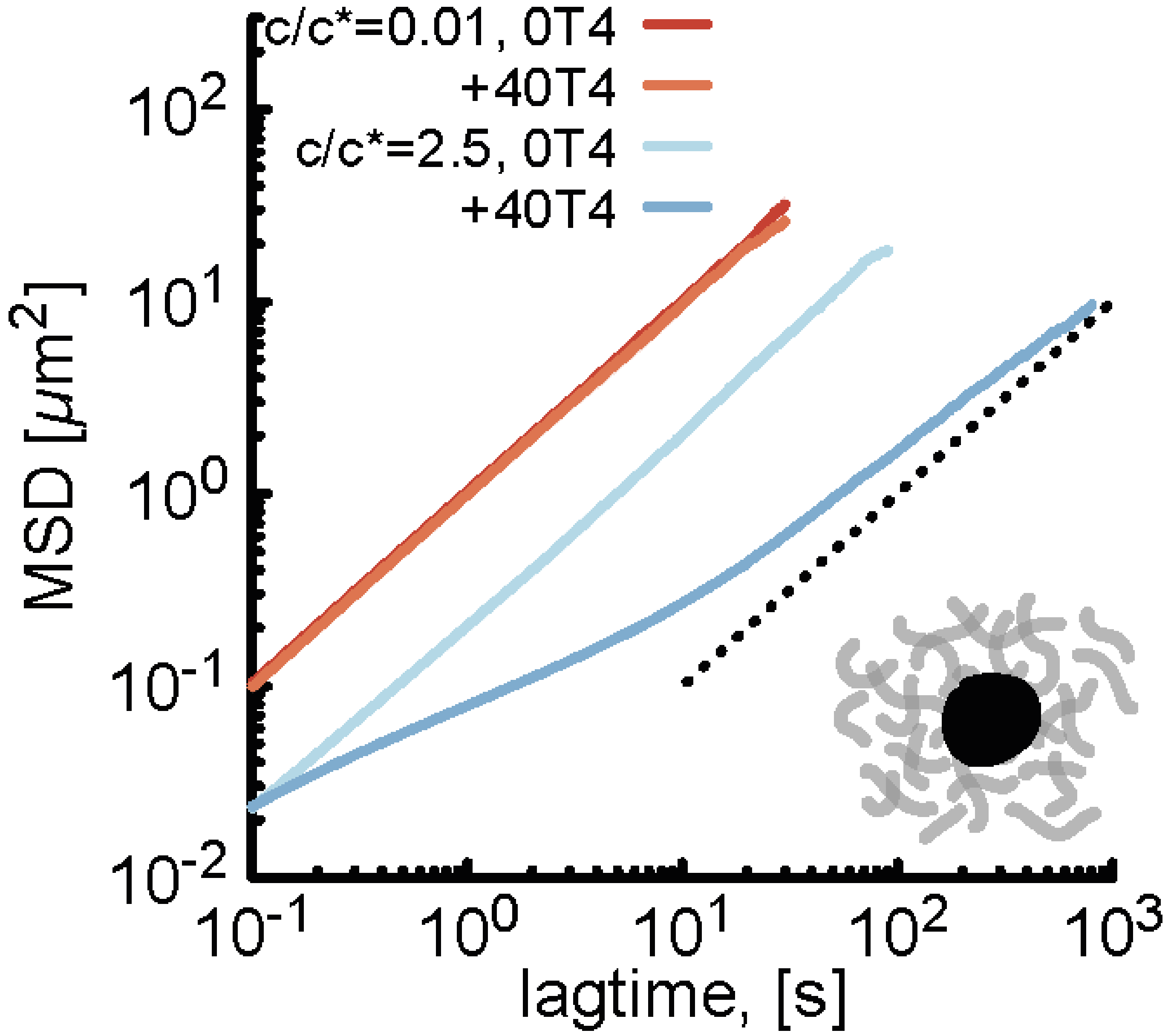
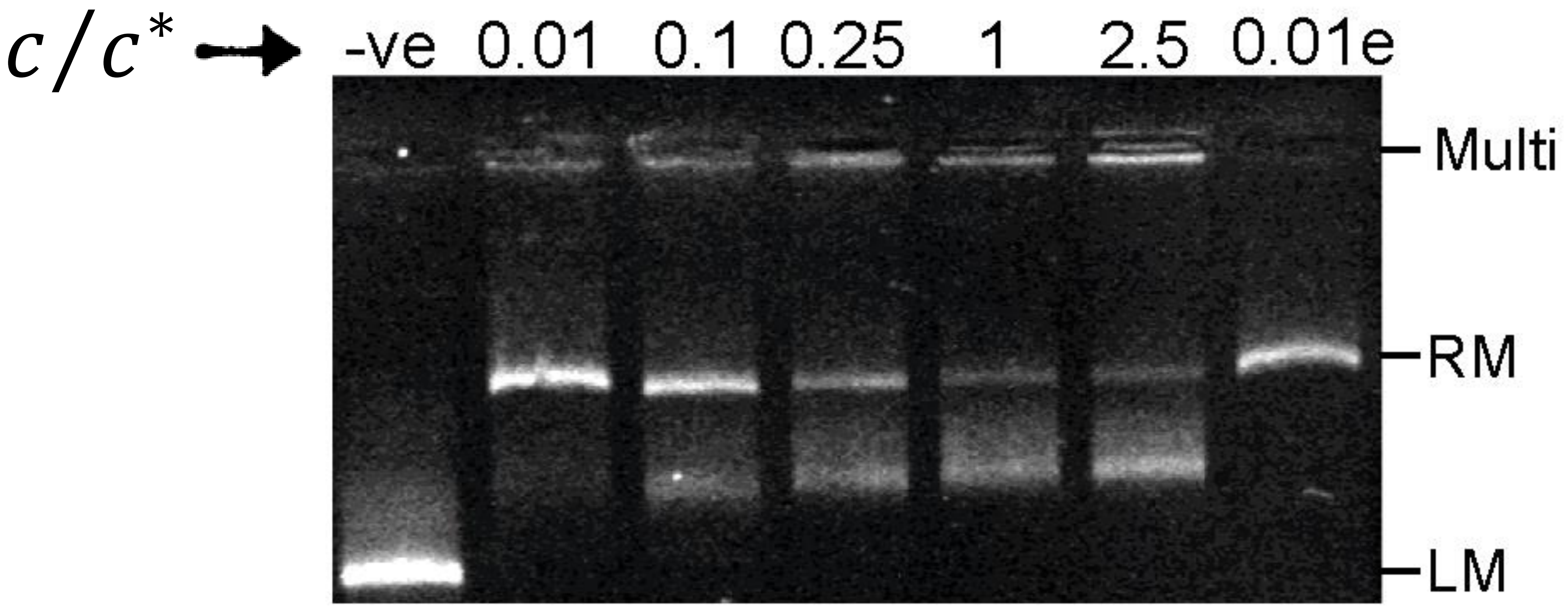


$$MSD(t) = \;< (r(t_o) - r(t_o + t))^2 >$$

$$D = \lim_{x \to \infty} MSD(t)/6t \qquad \eta = \frac{k_B T}{6\pi D r}$$

Micro-rheology



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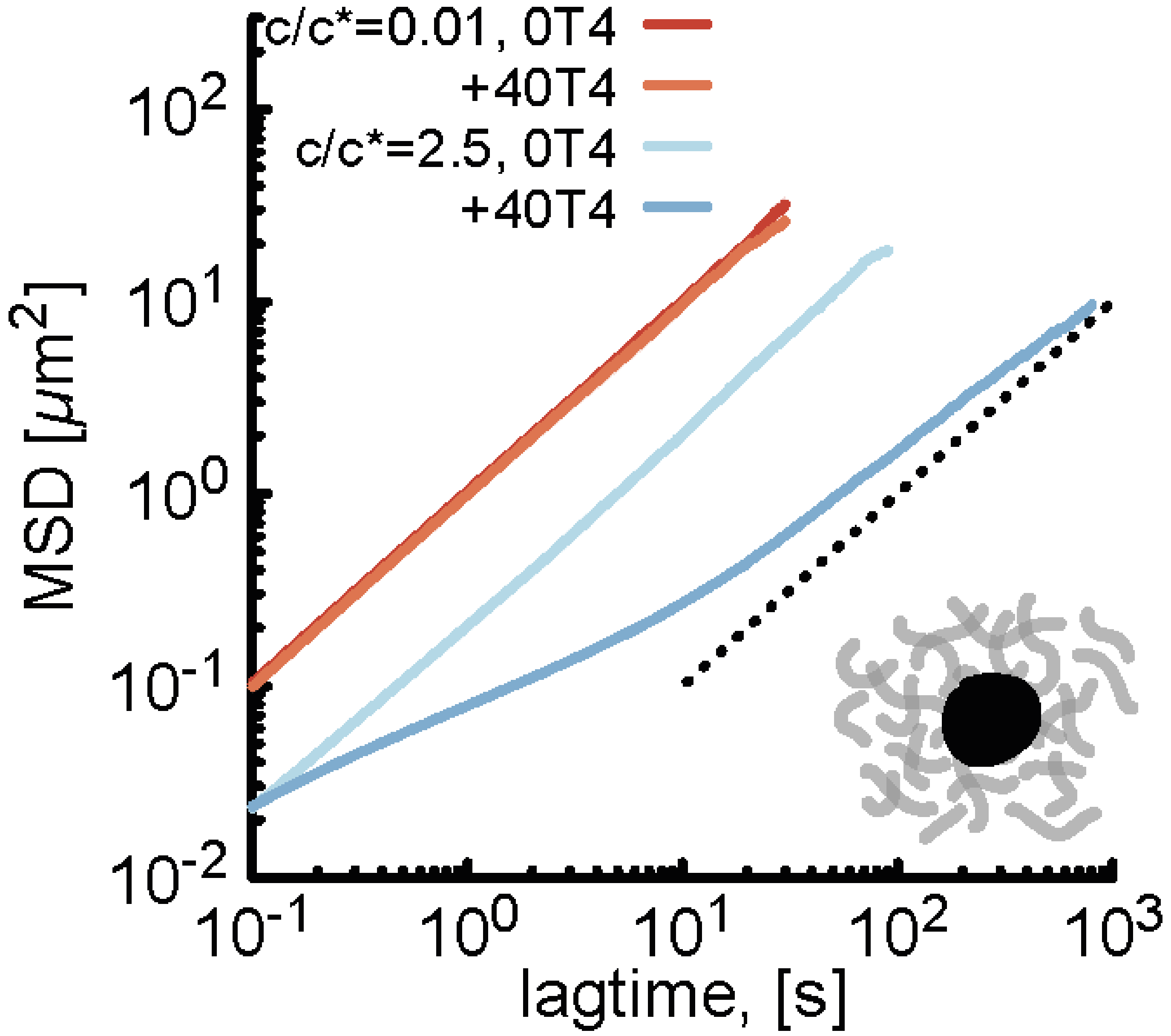

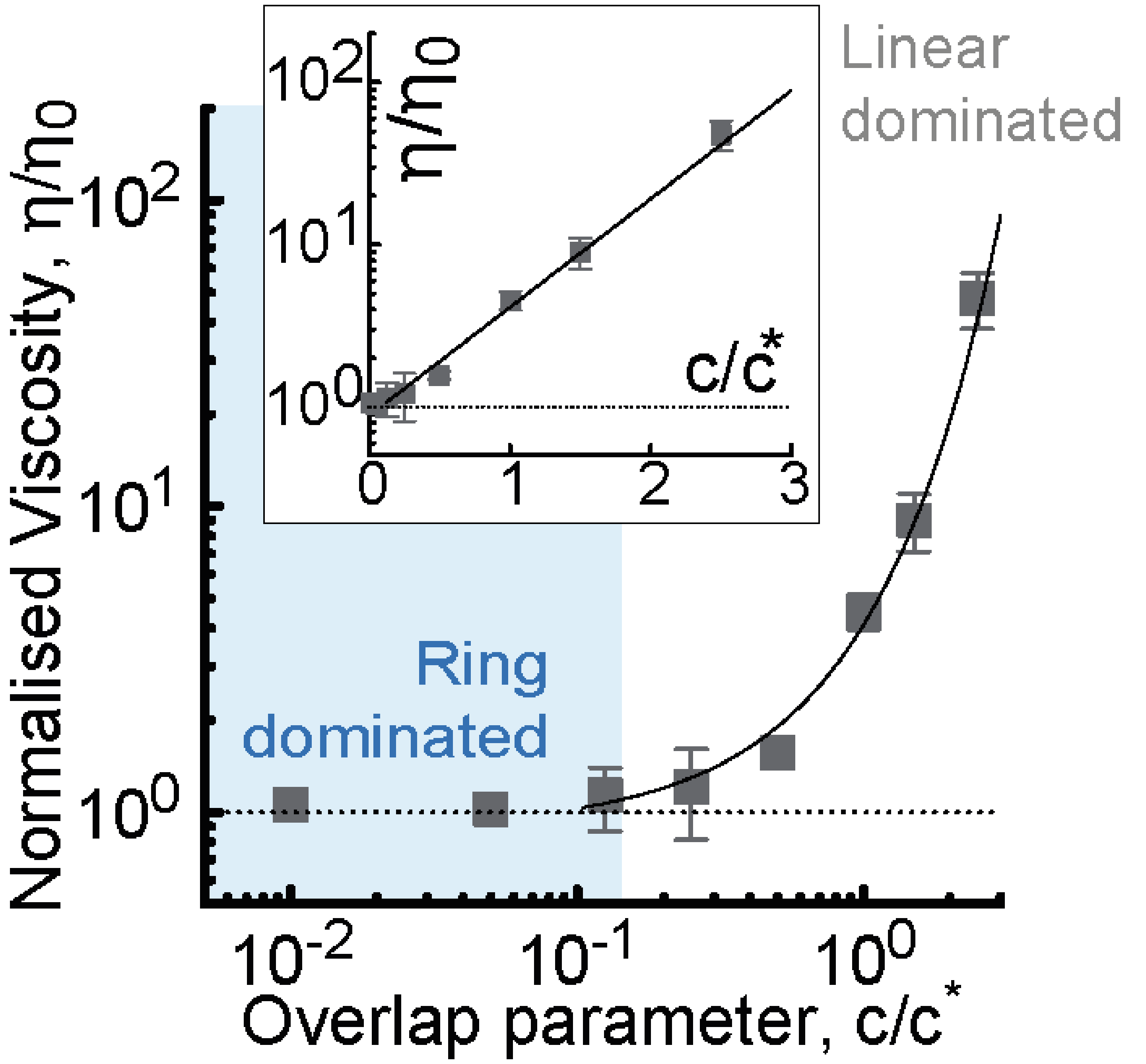

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Conclusions

- The key adimensional parameter controlling growth kinetics is $\kappa = 2\kappa_o / n_o \kappa_1$.
- Our results suggest that it may be possible to tune the final topological composition of ligated systems by judiciously choosing c/c*.
- It may be possible to couple dissipative DNA breakage reactions with ATP-consuming ligation to create dense solutions of self-sustained topologically active viscoelastic fluids.

Acknowledgements

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