Mesoscale simulations of stimuli-sensitive polymer networks

Alexander Alexeev

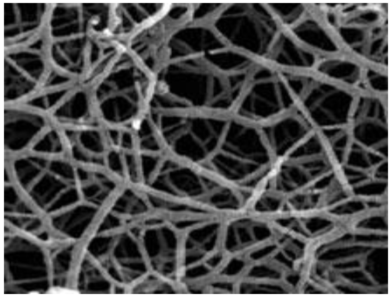
Complex Fluids Modeling and Simulation Group

The George W. Woodruff School of Mechanical Engineering
Georgia Institute of Technology

Polymer Networks

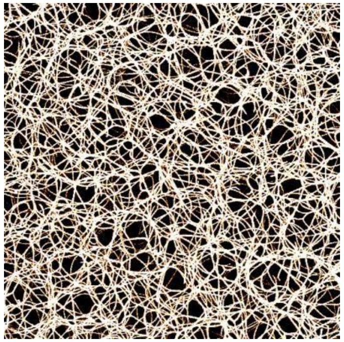
- **Types of polymer networks**
  - Natural (cytoskeletal structures)
  - Synthetic (hydrogels)
- **Properties of polymer networks**
  - Highly permeable (porosity ~ 0.75 − 0.98)
  - Extremely flexible (elastic modulus ~ 1 − 103 kPa)
  - Mechanically sturdy (support external loads)
  - Sensitive to external stimuli (light, pH, T, etc)
- **Applications**
  - Smart and responsive materials
  - Drug delivery
  - Tissue engineering
- **Goal**
  - Develop mesoscale model that can capture mechanical and transport properties of responsive polymer networks

Synthetic fibrous network



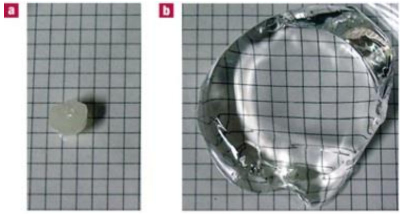
Tysseling-Mattiace *et al.*, J. Neuroscience, 2008

Actin network



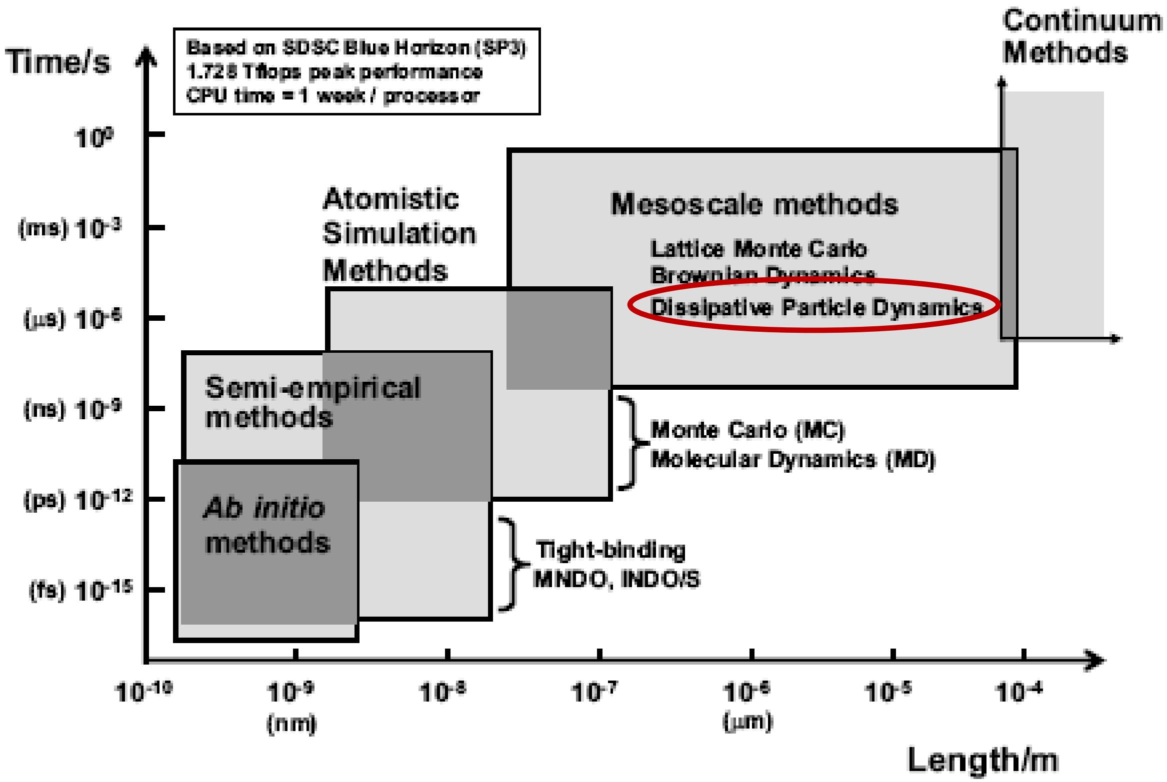
Schmoller *et al.*, Nature Communications, 2010

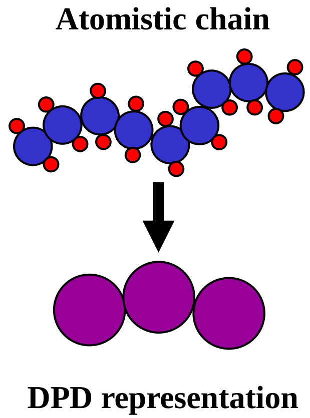
Gel swelling

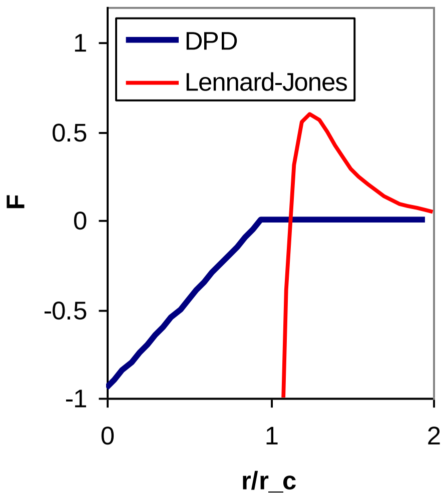


Ono *et al.*, Nature Materials, 2007

Simulation Approach





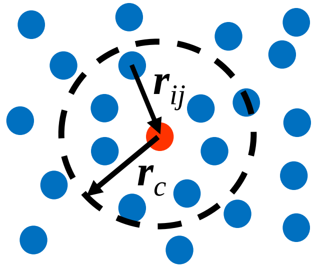


- **Dissipative Particle Dynamics**
  - ☞ Use soft potential to represent cluster of atoms
  - – Allow simulations with larger time/length scales

Dissipative Particle Dynamics (DPD)

- **Newtonian time evolution of many-body system (similar to MD)**

$$\frac{d\mathbf{r}_i}{dt} = \mathbf{v}_i \qquad \frac{d\mathbf{v}_i}{dt} = \sum \left(F_{ij}^C + F_{ij}^D + F_{ij}^R \right) \hat{\mathbf{r}}_{ij}$$



  - ☞ Repulsive force
    - – Accounts for compressibility

$$F_{ij}^C = a_{ij} \left(1 - r_{ij} / r_c \right)$$

  - ☞ Dissipative drag force
    - – Mimics viscosity

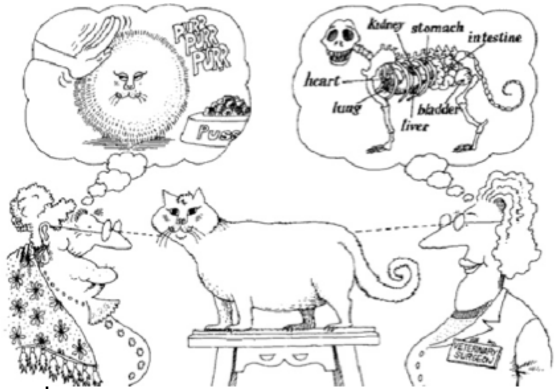
$$F_{ij}^D = -\gamma \left(1 - r_{ij} / r_c \right)^2 \left(\hat{\mathbf{r}}_{ij} \cdot \mathbf{v}_{ij} \right)$$

  - ☞ Stochastic force
    - – Represent thermal fluctuations

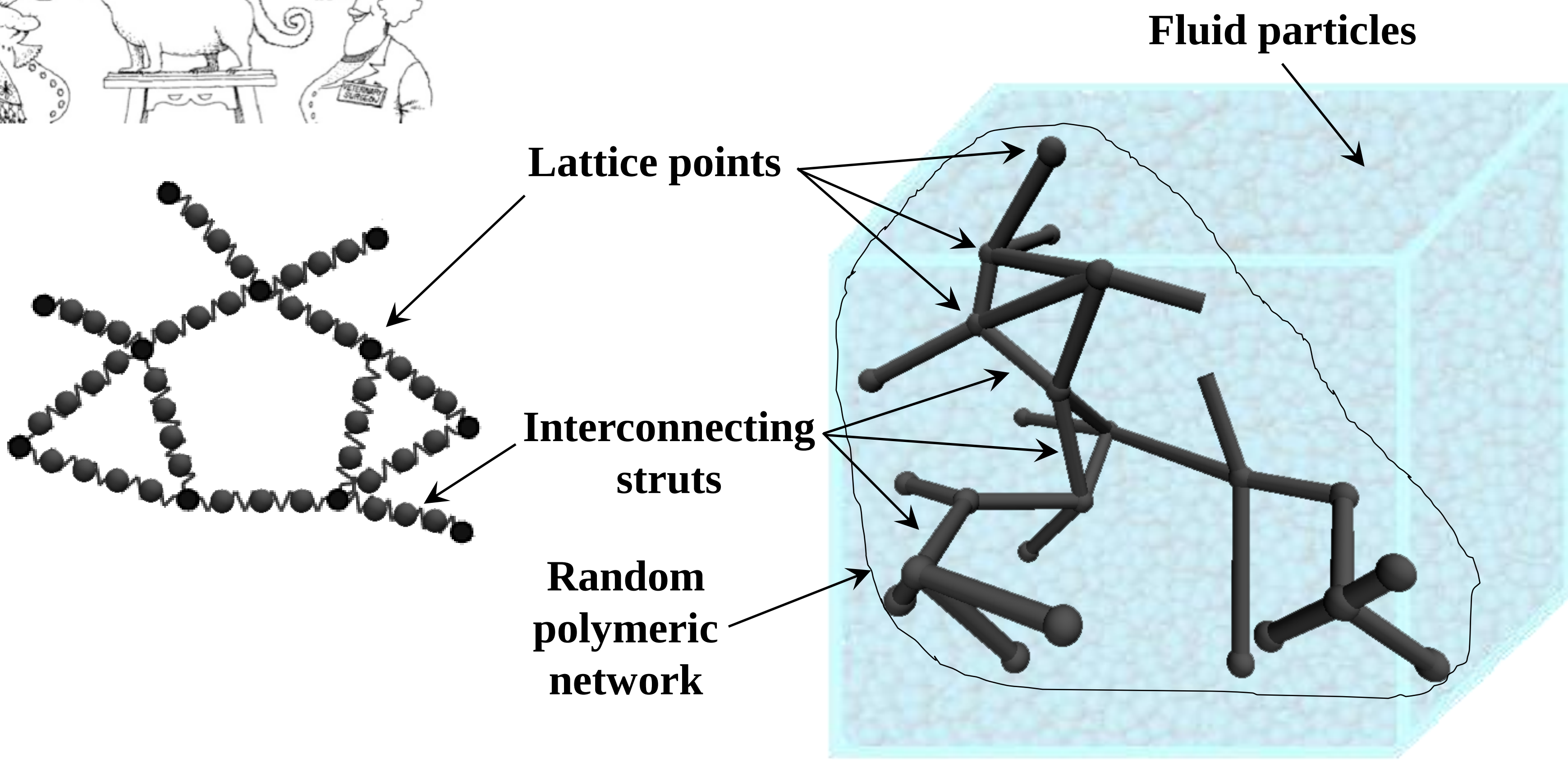
$$F_{ij}^R = \sqrt{2\gamma k_B T} \left(1 - r_{ij} / r_c \right) \zeta_{ij} \Big/ \sqrt{\Delta t}$$

- **Pair-wise and central forces to preserve hydrodynamics**

- **Departure from Molecular Dynamics (MD) :**
  - ☞ Soft conservative interaction potential
  - ☞ Coarse-grained in time and space (“fluid elements”)



Mesoscale Model of Polymer Network



- **Model polymeric networks as random lattice of interconnected filaments**
  - ☞ Replicates microscopic architecture at mesoscale level

Polymer Network Model

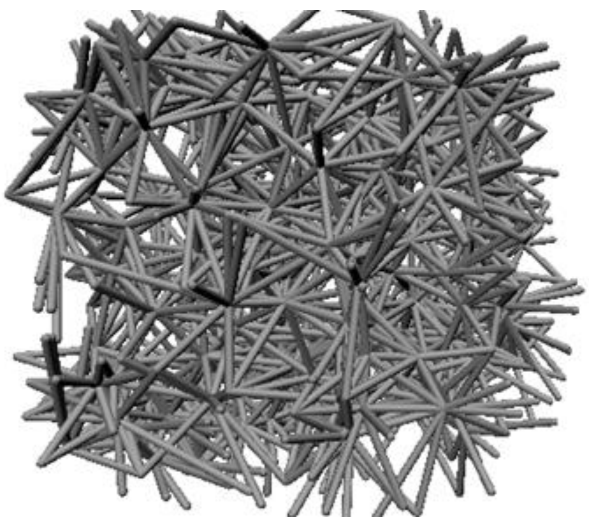
- **Network is created in two steps**
  - Randomly distribute *N* cross-linking nodes in simulation box
  - Connect each node to the *C* closest nodes

$N = \text{Number of corss-linking nodes}$

$C = \text{Average connectivity (cross-linking density)}$

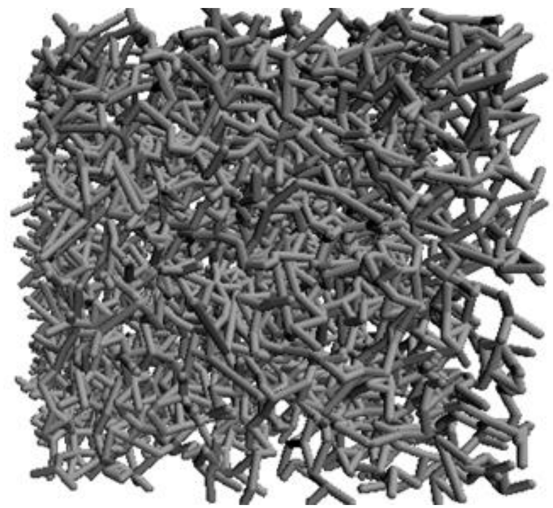
$$\text{Porosity}(\varepsilon) = \frac{\text{Volume of voids}}{\text{Total volume}}$$

$N = 250 \qquad C = 12$



$\varepsilon \approx 0.81$

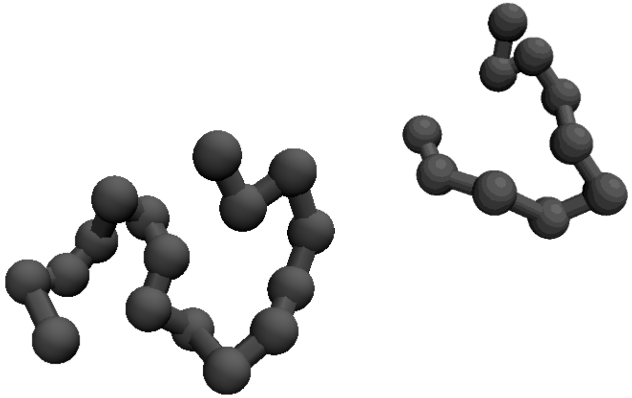
$N = 2000 \qquad C = 3$



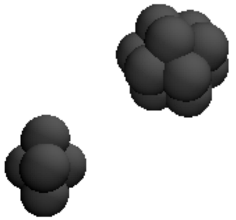
- **Accurate control over network properties**

Macromolecules and Nanoparticles

- **Bead-spring model to model polymer chains**
  - FENE spring to model flexible polymers
  - Harmonic stretching and angle (triple) potentials to model semi-flexible polymers



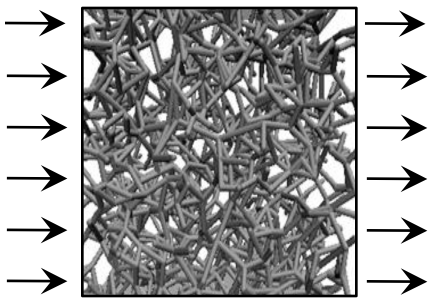
- **DPD beads with fixed relative position to model rigid particles**
  - Size is characterized by effective hydrodynamic radius

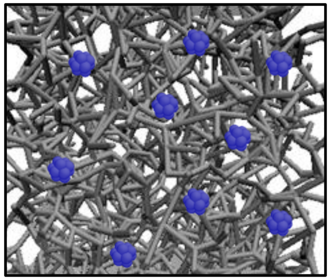


- **DPD potentials account for interactions with surroundings**

Transport Through Polymer Networks

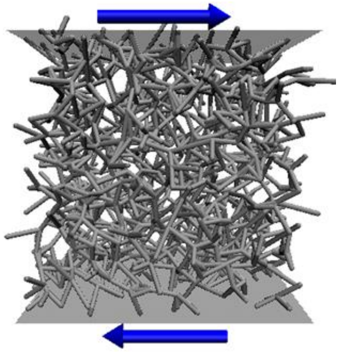
- **Study transport through polymer networks**
  - Permeation
  - Self-diffusion
  - Particle diffusion
  - Chain diffusion





- **Quantify dependence of transport properties on network geometry**

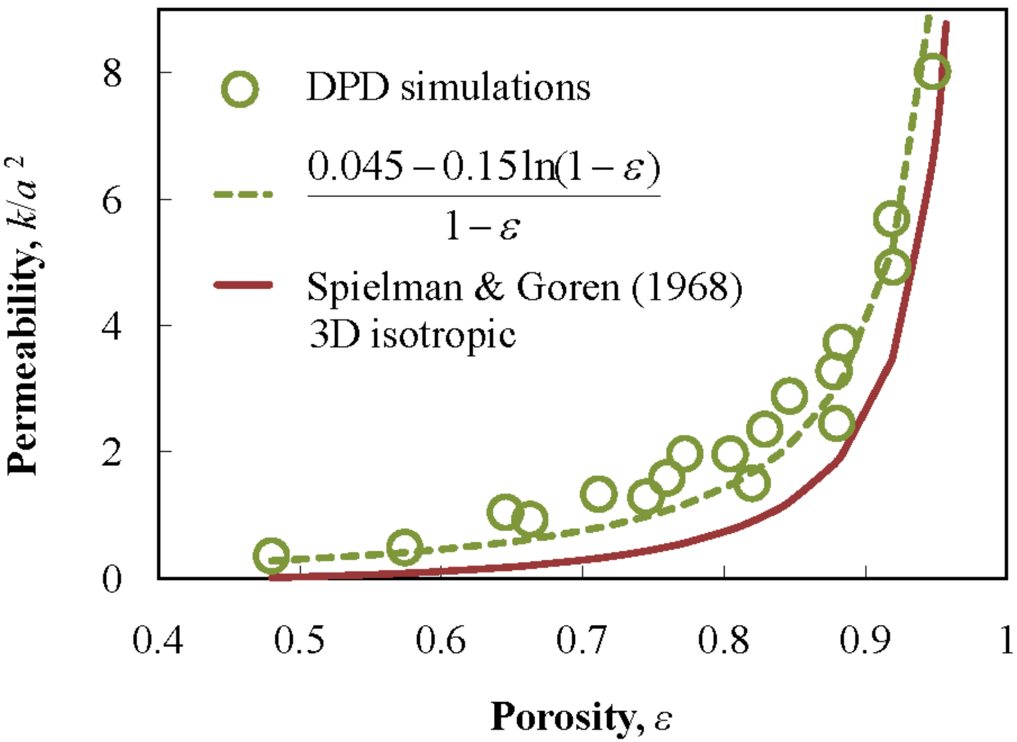
- **Probe effect of mechanical deformation on permeation and diffusion**

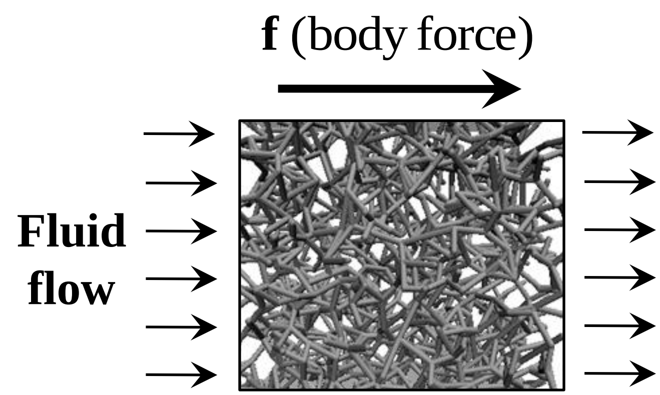


Network Permeability

$a =$ Radius of filaments

$$\varepsilon = \frac{\text{Volume of voids}}{\text{Total volume}}$$

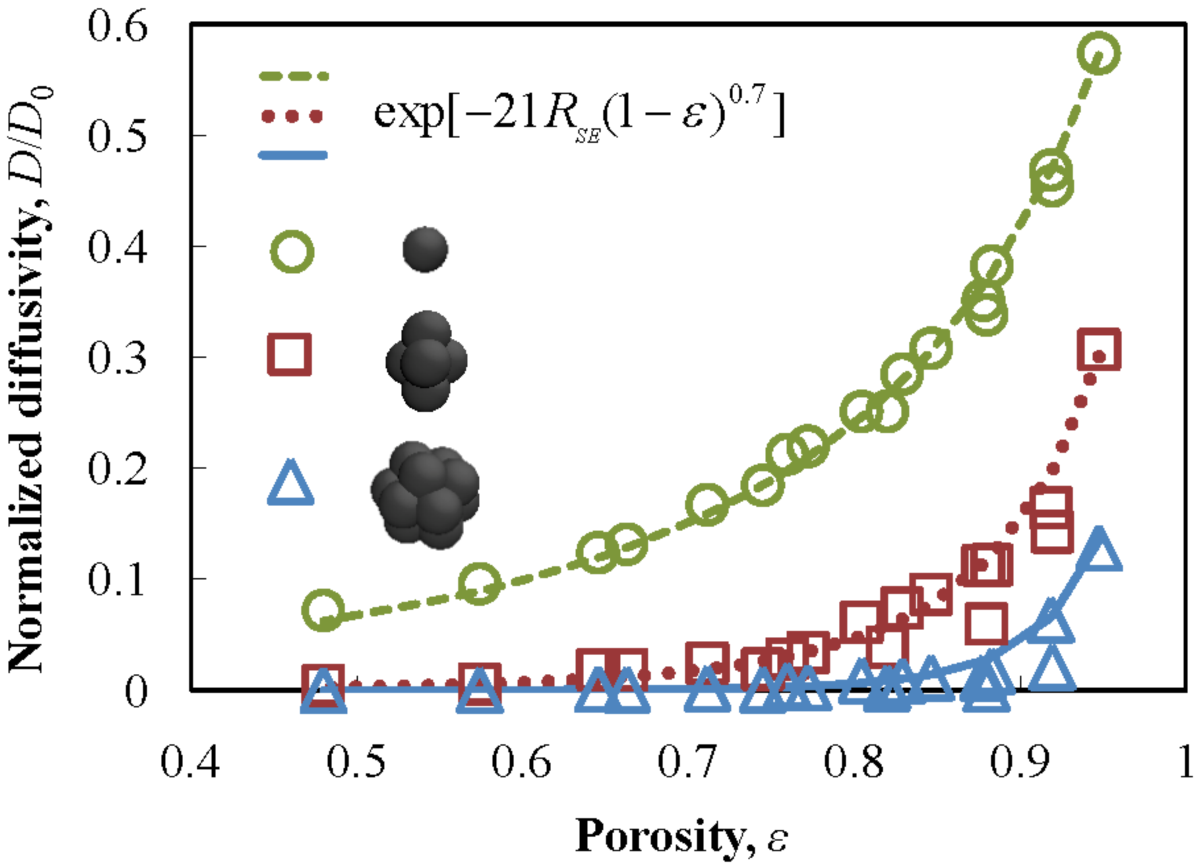




$$\text{permrability}(k) = \frac{\mathbf{q}\nu}{\mathbf{f}}$$

- **Normalized permeability is independent of network internal structure**
  - ☞ Solely function of fraction of void volume (porosity)
  - ☞ Good agreement with theory and experiment

Diffusion of Rigid Particles



$$\frac{D}{D_0} = \exp[-\alpha R^{\delta}(1-\varepsilon)^{\nu}]$$

Phillies, J. Chem. Phys., 1989

Phillies *et al.*, J. Chem. Phys., 1989

$$\frac{D}{D_0} = \frac{D_{\text{with network}}}{D_{\text{withoutnetwork}}}$$

$\nu = 0.7$

experiments of

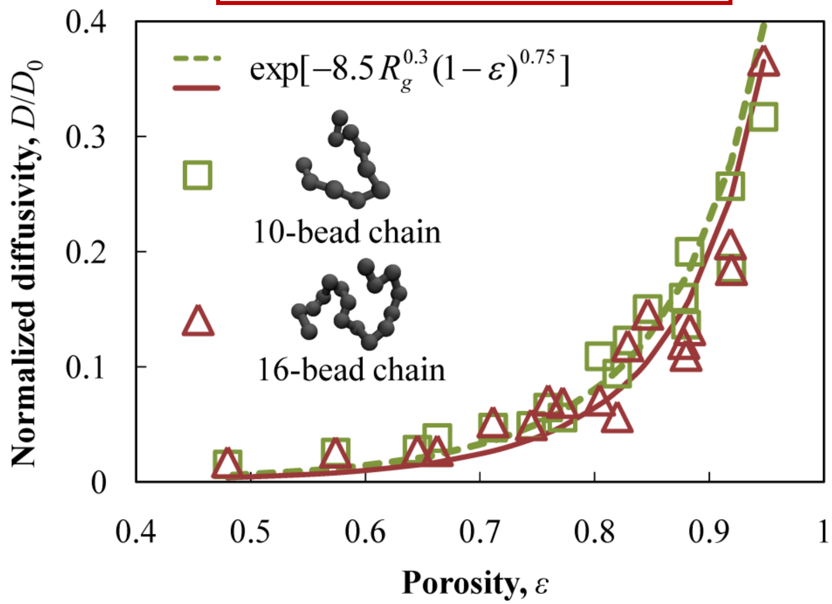
Seiffert & Oppermann, Polymer, 2008

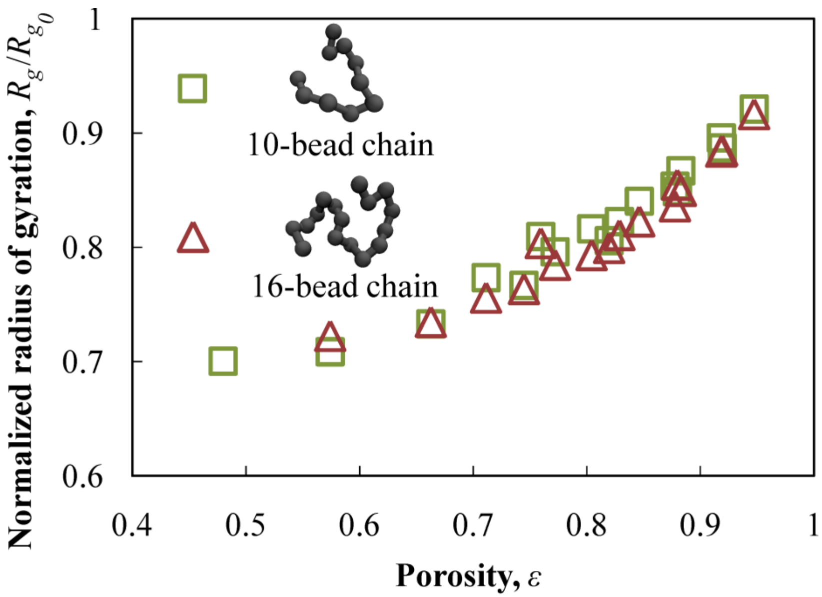
- ❑ **Normalized diffusivity is also solely function of porosity**
- ❑ **Good agreement with hydrodynamic scaling model and experiment**

Diffusion of Polymer Chains

$\nu = 0.8$
experiments of
Seiffert & Oppermann, Polymer, 2008

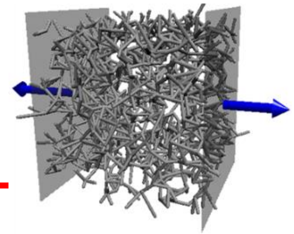
$$\frac{D}{D_0} = \frac{D_{\text{with network}}}{D_{\text{withoutnetwork}}} = \exp[-\alpha R^{\delta}(1-\varepsilon)^{\nu}]$$

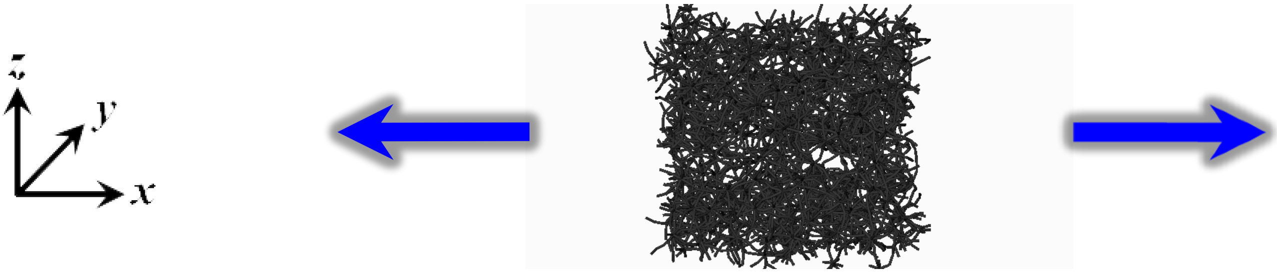


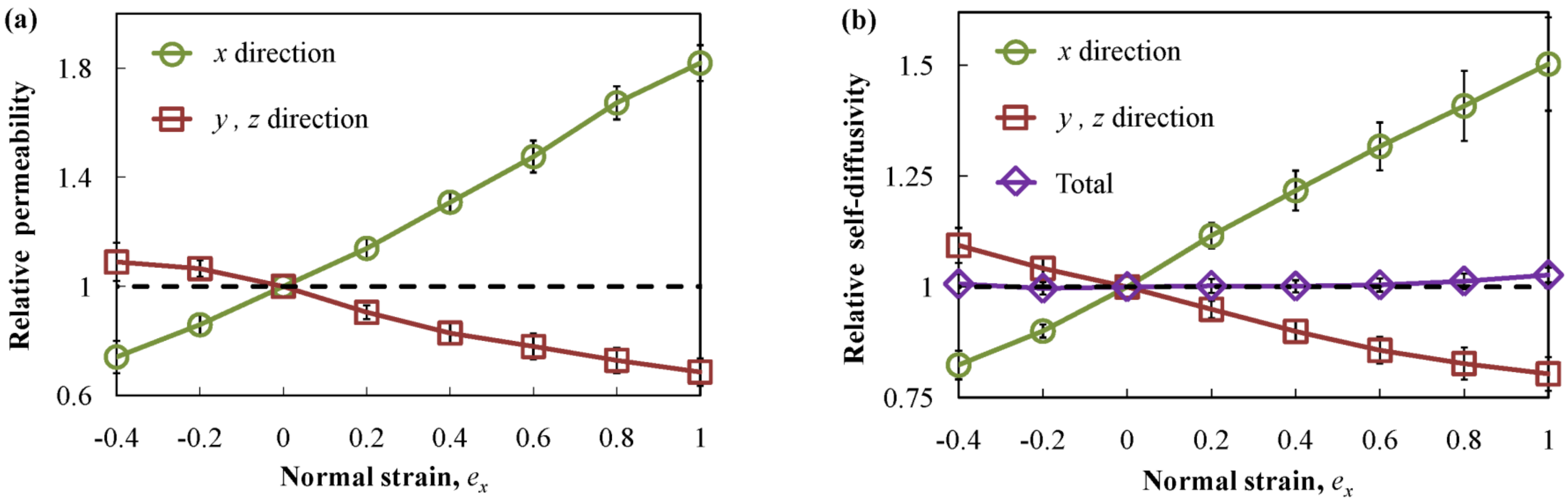


- ❑ **Good agreement with theory and experiment**
- ❑ **Smaller diffusion coefficient for particles comparing to polymer chains**
  - ☞ Change in radius of gyration of polymer chains

Transport Under Axial Deformation

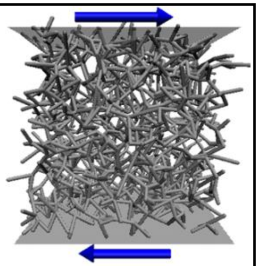


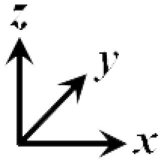


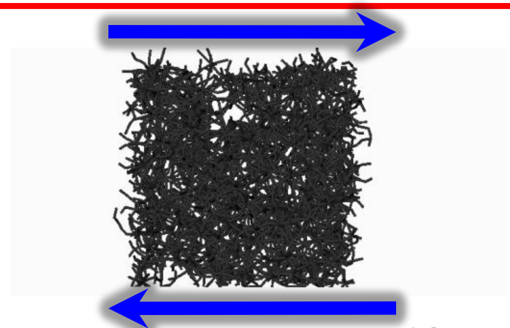


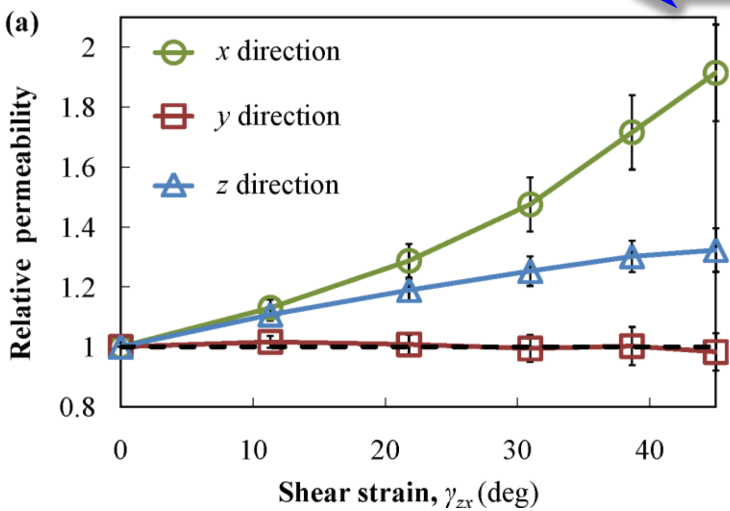
- **Data averaged over 18 networks (*N*=250,500,1000 & *C*=4,6,8,10,12,14)**
- **Stretching enhances permeation and diffusion in direction of deformation**
  - ☞ Opposite effect in transverse direction
- **Total diffusivity remains unchanged under axial deformation**

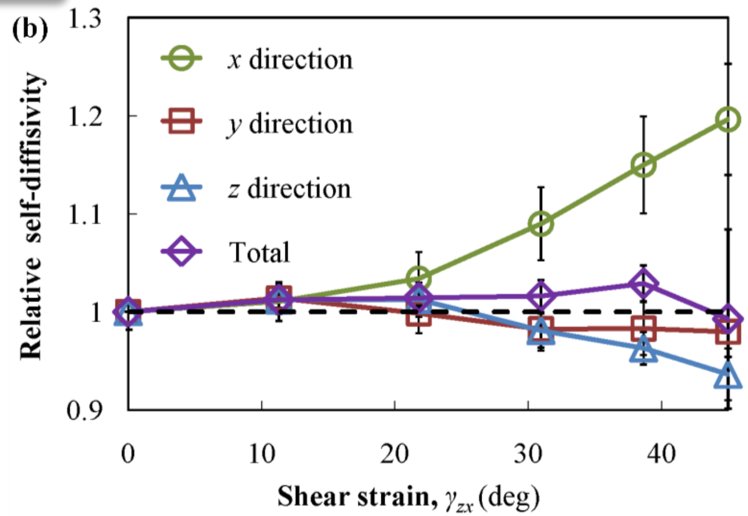
Transport Under Shear Deformation









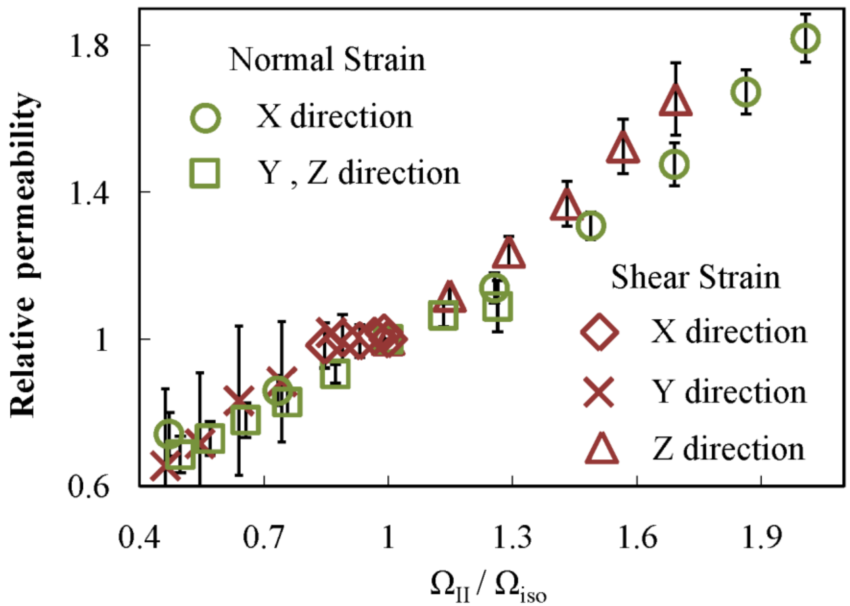


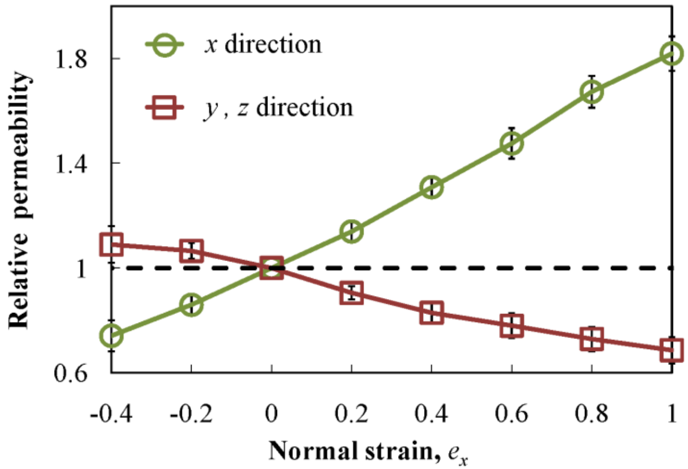
- **Data averaged over 18 networks (*N*=250,500,1000 & *C*=4,6,8,10,12,14)**
- **Permeability in *y* direction remains unchanged under shear deformation**
  - ☞ Filaments rotate in *xz* plane
- **Total diffusivity remains unchanged under shear deformation**

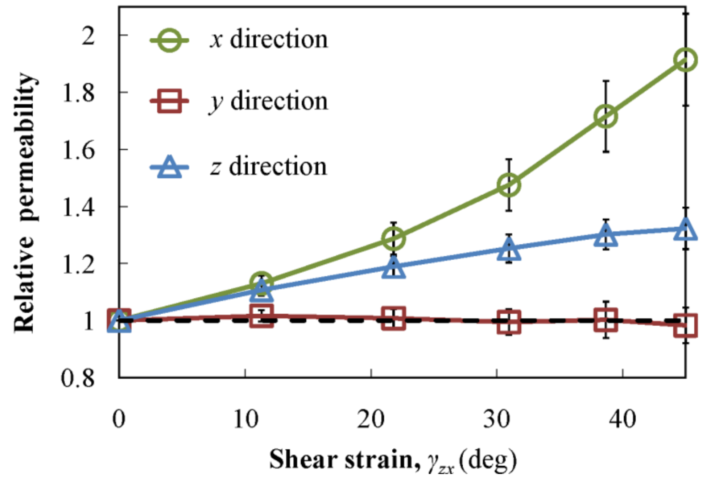
Permeability in Principal Direction

- **Characterize degree of alignment by second order orientation tensor**

Relative permeability in principal directions of orientation tensor



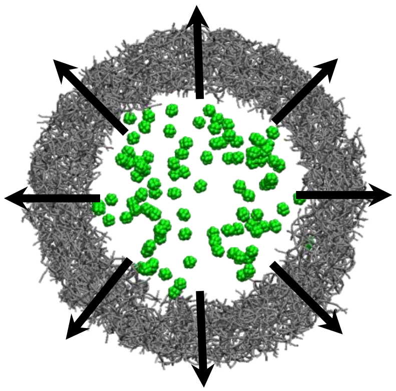




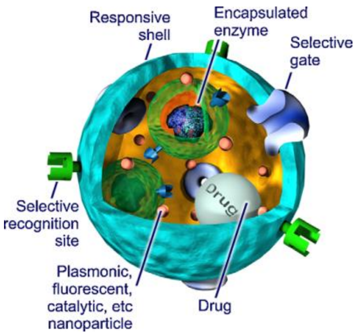
- **All data collapses into single master curve**
  - ☞ Nearly linear dependence on magnitude of orientation tensor eigenvalues

Release From Responsive Capsules

- **Release from drug delivery microcapsules**
  - Controllable
  - Non-destructive
  - Sensitive to external stimuli



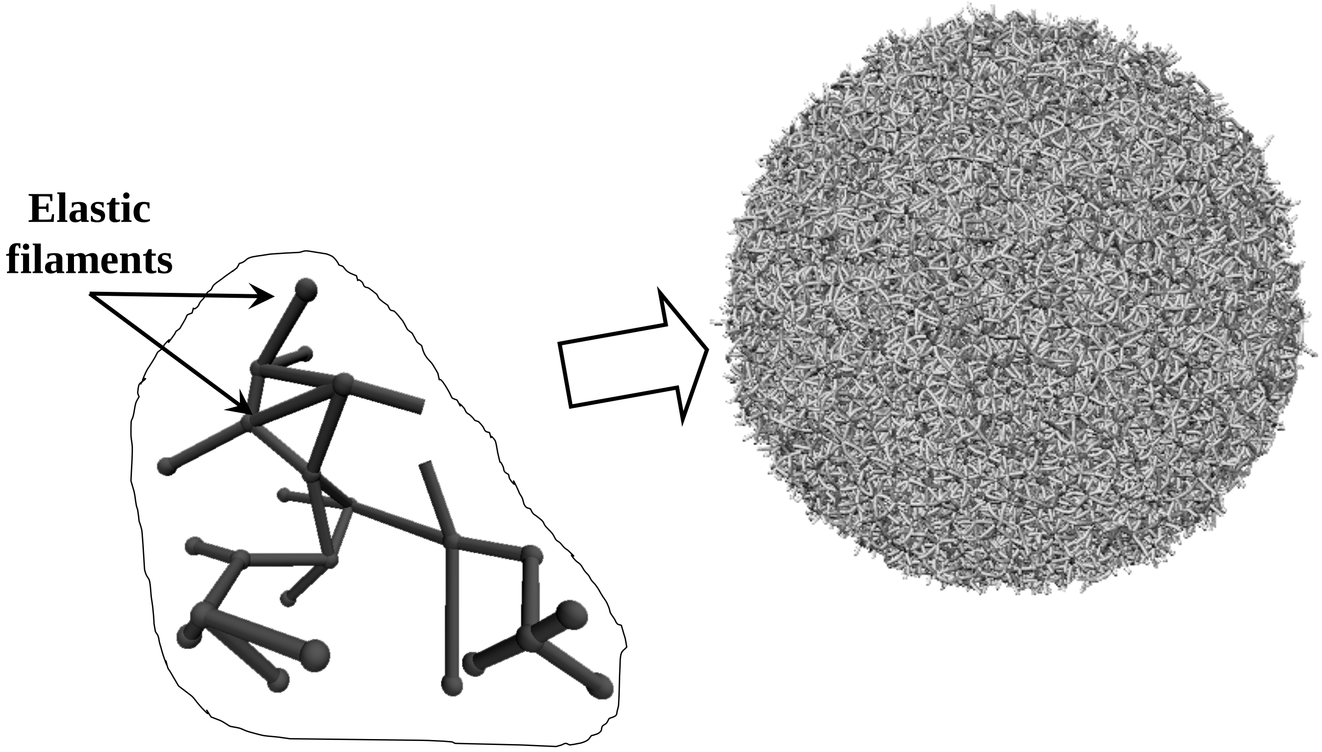
- **Study release from responsive microgel capsules**
  - Swelling/deswelling volume transitions
- **Mesoscale model for responsive polymer networks (gels)**
  - Micromechanics of polymer network
  - Explicit solvent
  - Diffusive and advective transport
  - Swelling/deswelling volume transition



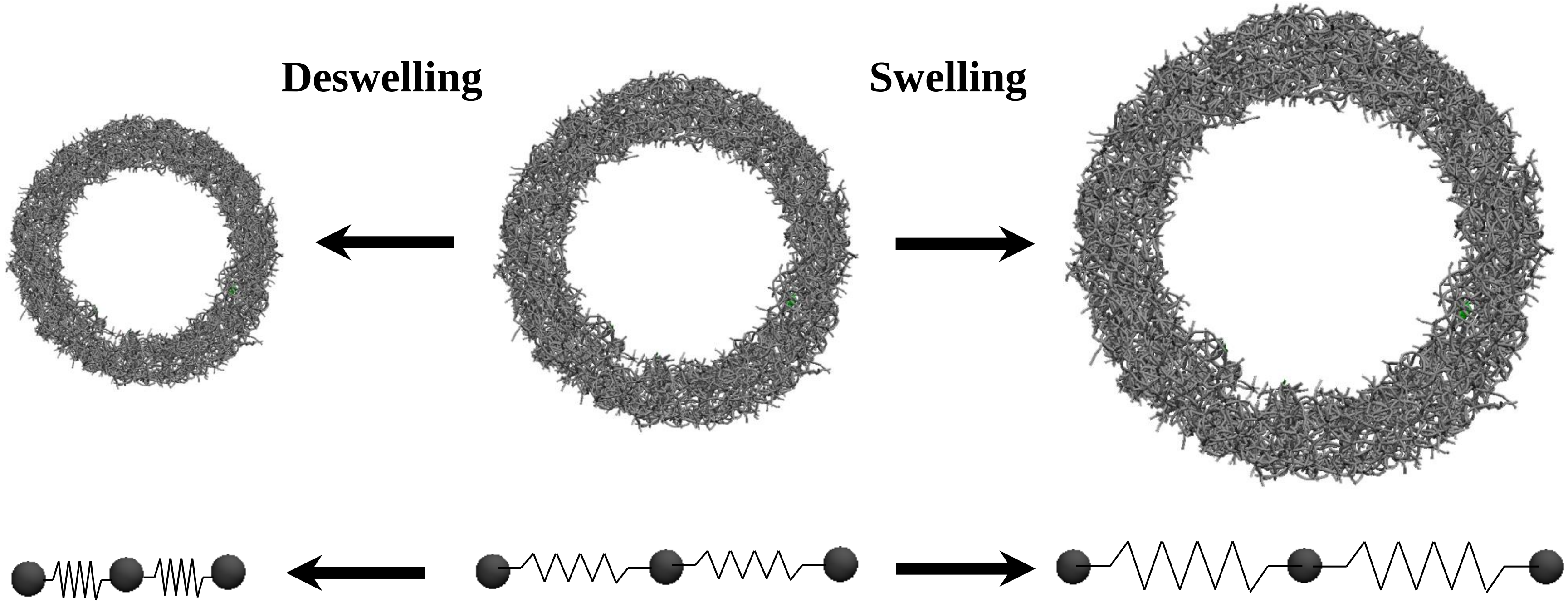
Motornov *et al.*
Prog. Polym. Sci., 2010

Responsive Microgel

- **Random network of interconnecting elastic filaments**
  - ☞ Filaments of DPD beads connected by stretching and bending springs
  - ☞ Spherical capsule is formed by trimming homogeneous network



Modeling Gel Volume Transition



- **Network volume transition is modeled by varying equilibrium length of network filaments**
  - ☞ Accounts for internal stresses that force network to shrink or expand
    - – Increase equilibrium length of springs to model swelling
    - – Decrease equilibrium length of springs and strength of DPD potentials to model deswelling

Swelling Kinetics of Spherical Capsules

- Swelling kinetics is set by balance between hydrodynamic and elastic forces

$$\tau_{sphere} = \frac{R_{final}^2}{\pi^2 D_0}$$

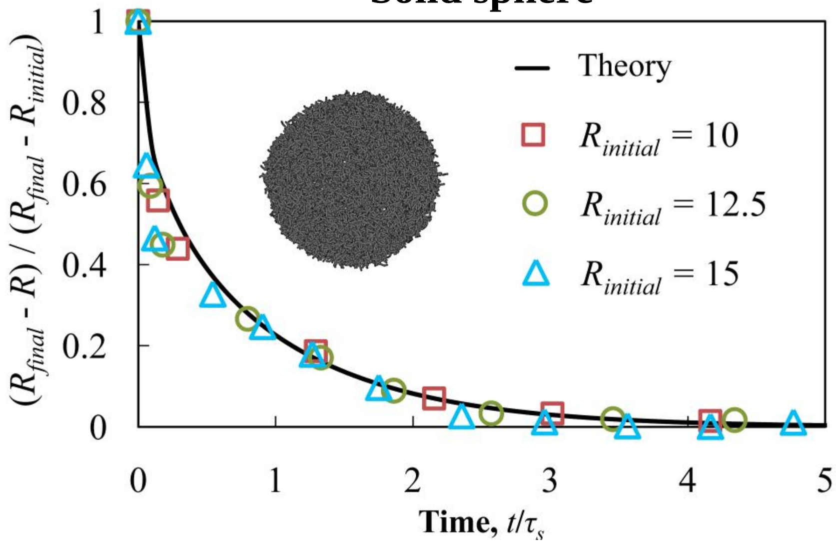
Tanaka and Fillmore, J. Chem. Phys., 1979

Tanaka's model ($t > \tau$): $$\frac{R_{final} - R}{R_{final} - R_{initial}} \cong \exp(t/\tau)$$

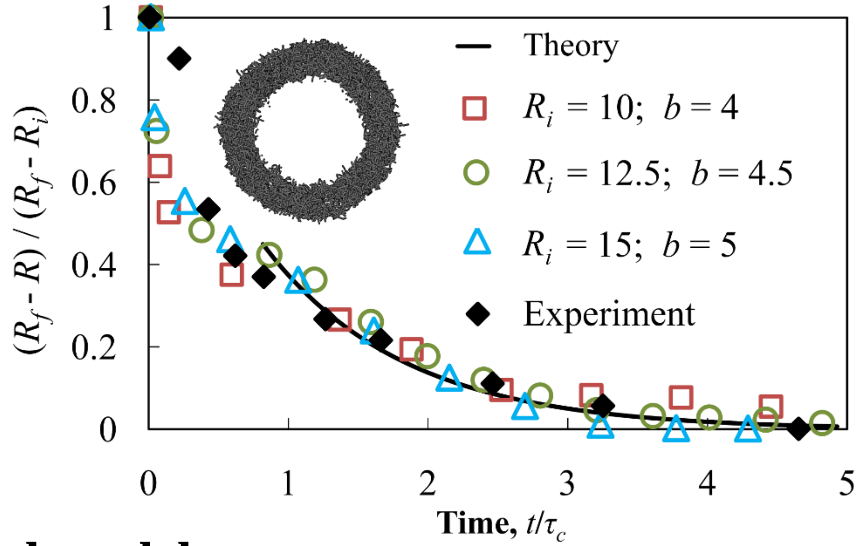
$$\tau_{capsule} = \frac{R_{final}^2}{9 D_0}$$

Wahrmund *et al.*, Macromolecules, 2009

Solid sphere

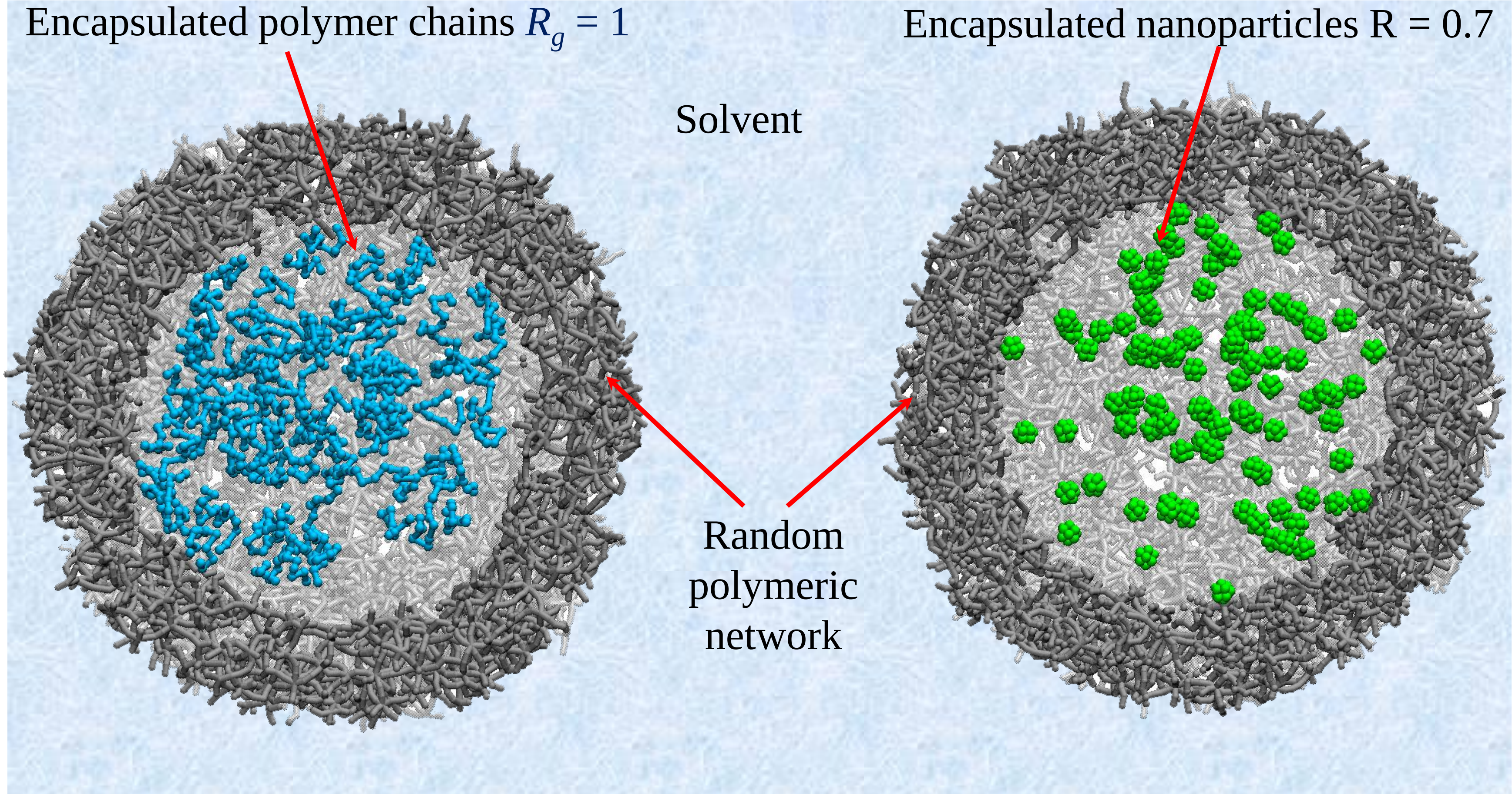


Hollow sphere



- Very good agreement with theoretical models
- Weak dependence of capsule relaxation time on the membrane thickness

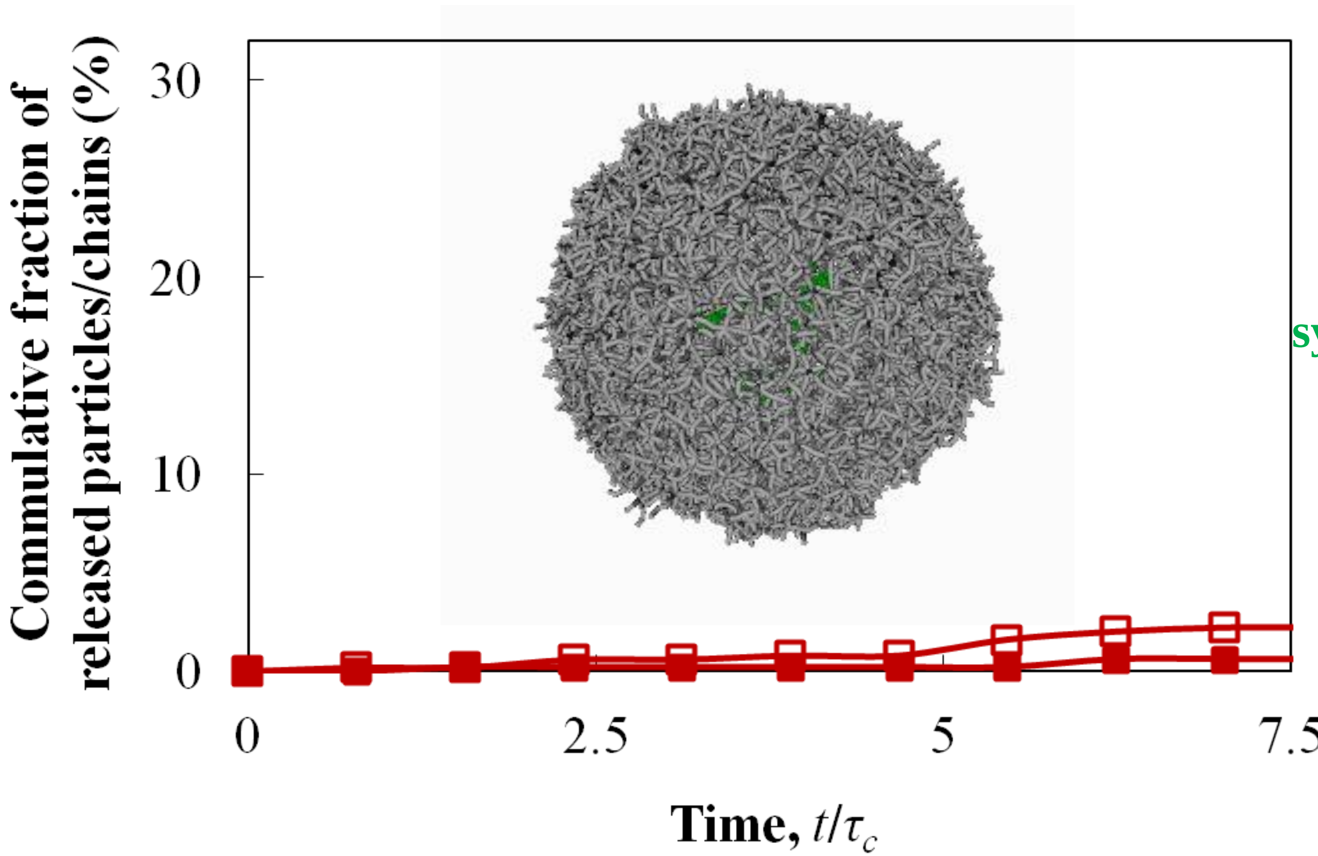
Capsules Filled With Particles and Polymer Chains



- **Probe release of macromolecules and nanoparticles from responsive microgel capsules**

Release From Capsules at Initial Equilibrium

Filled symbols for chains $R_g = 1$



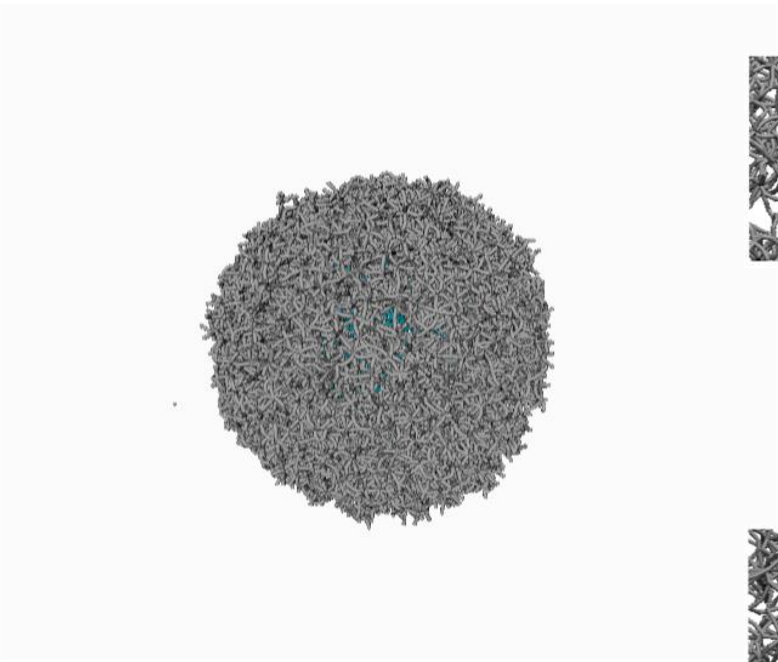
Empty symbols for particles $R = 0.7$

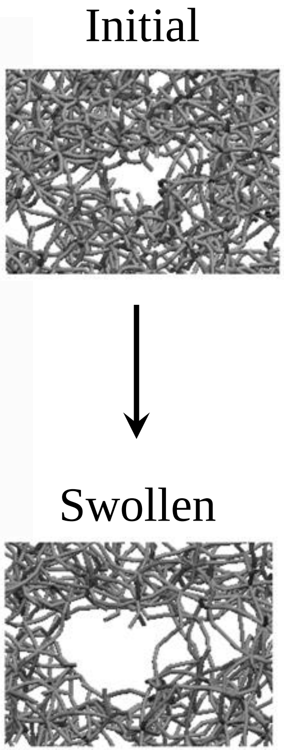
- ❑ **No release from capsule at initial state**
  - ☞ Characteristic size of solutes is comparable with network average mesh size

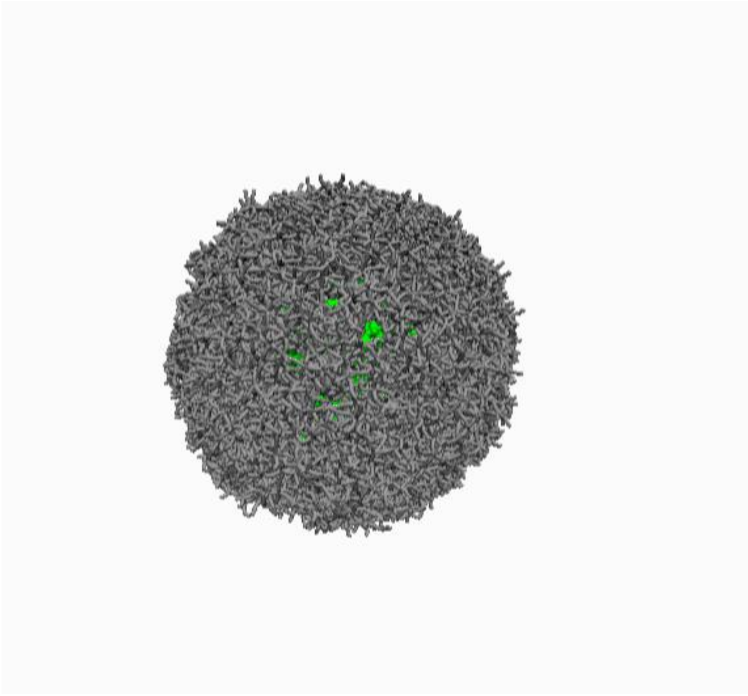
Release From Swelling Capsules

Capsule with macromolecules

Capsule with nanoparticles



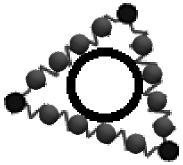


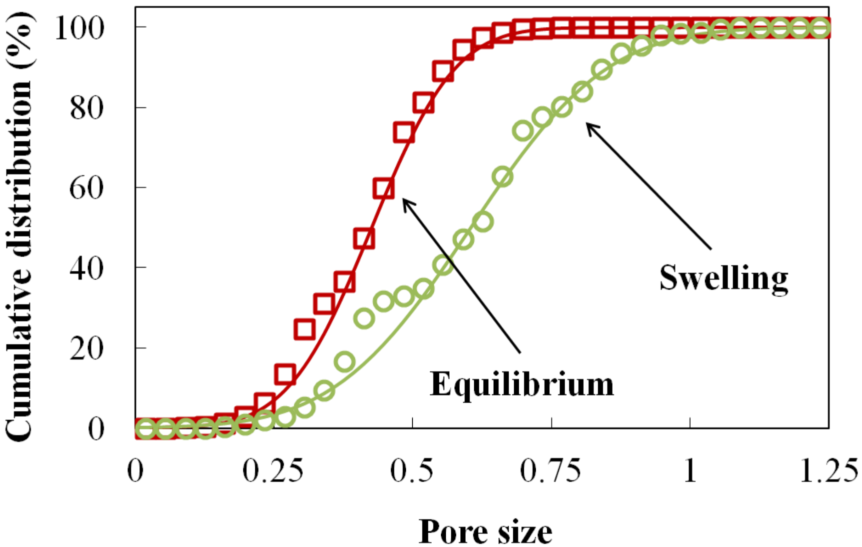


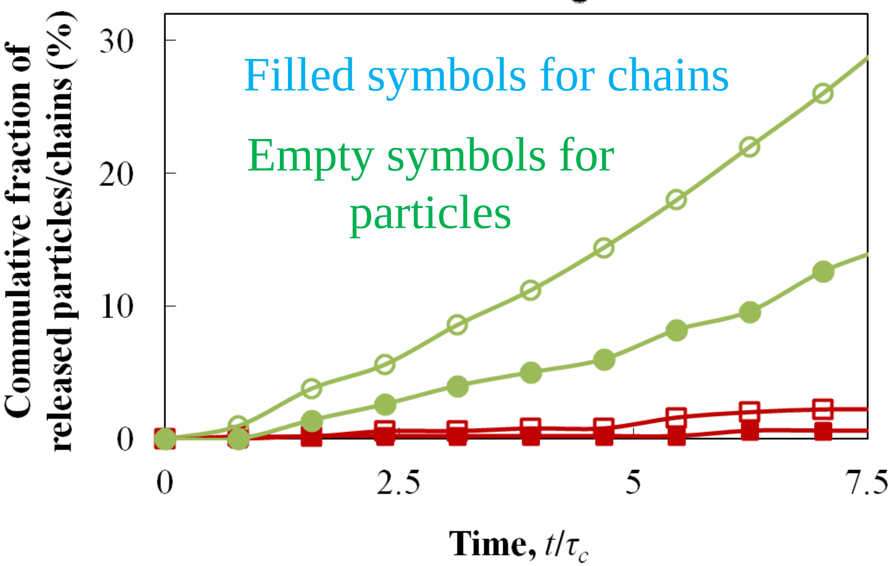
- **Capsule swelling leads to increase in network average pore size**
  - ☞ Gives rise to diffusion-controlled release

Release From Swelling Capsules

Pore size = Radius of the largest circle contained
in a triangle formed by three filaments





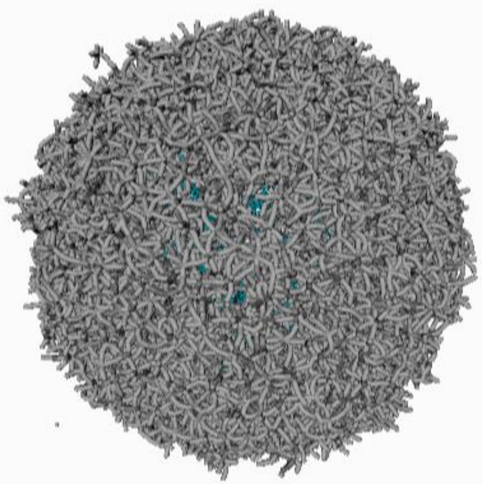


- **Steady release during swelling**
  - Defined by diffusion through capsule shell including entropic barrier to enter membrane
    - Polymer chains release slower than rigid nanoparticles
  - Agrees well with 1D diffusion through spherical shell
    - Constant release rate

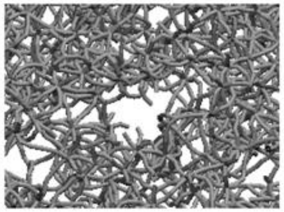
Release From Deswelling Capsules

Capsule with macromolecules

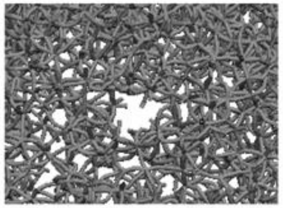
Capsule with nanoparticles

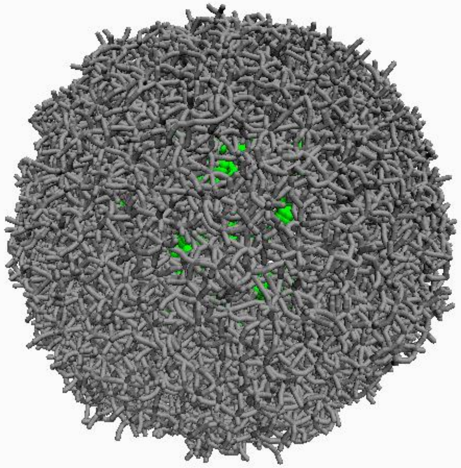


Initial



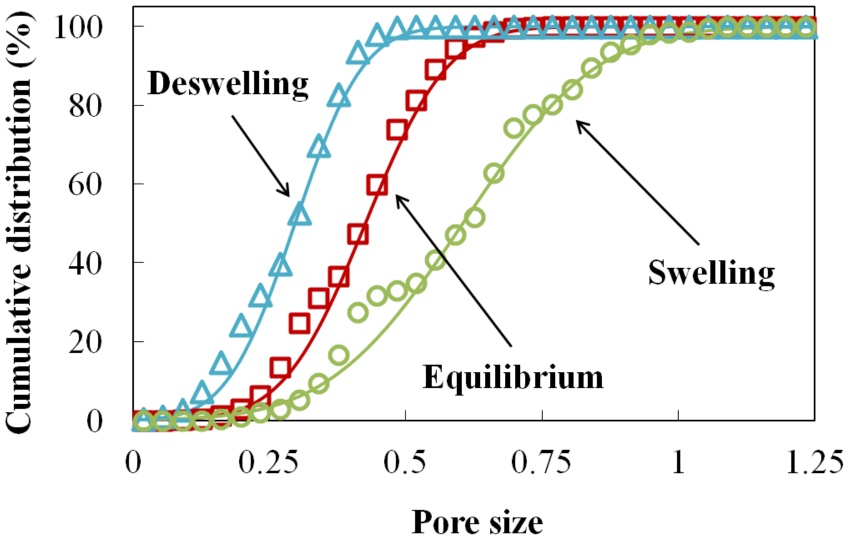
Deswelling

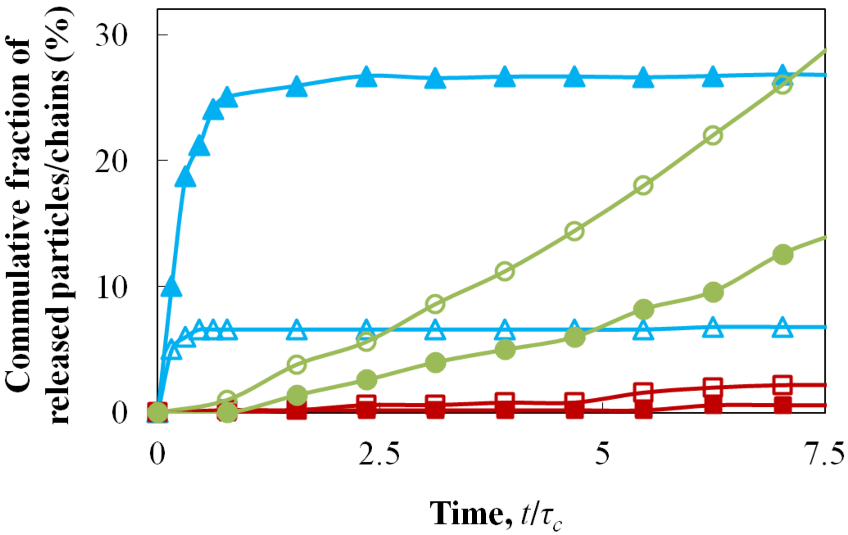


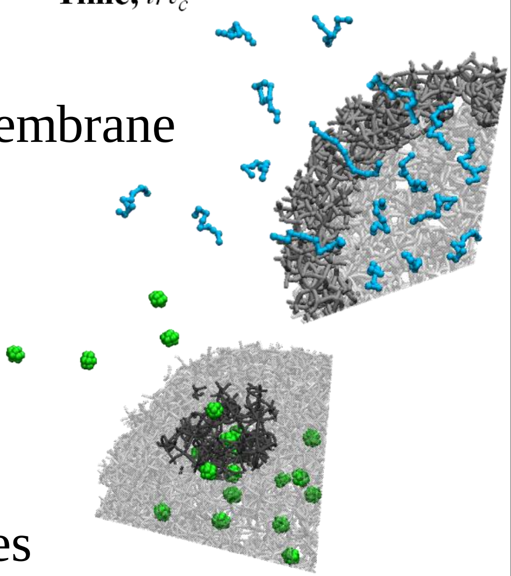


- **Capsule deswelling leads to squeezing flow from capsule interior**
  - ☞ Results is rapid hydrodynamic release

Release From Deswelling Capsules



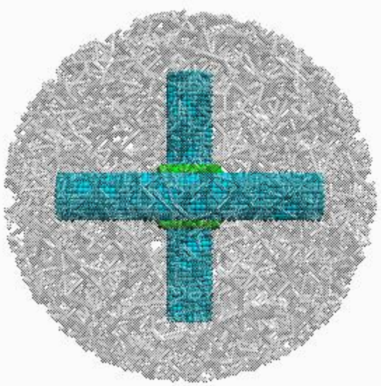




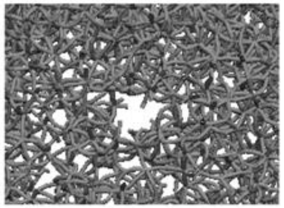
- ❑ **Rapid discharge of solutes followed by no release**
  - ☞ Driven by fluid flow from inside capsule through membrane
- ❑ **Polymer chains release faster than nanoparticles**
  - ☞ Polymers unfold and reptate through membrane
- ❑ **Precise control of release amount**
  - ☞ Defined by volume of released fluid
  - ☞ Release is limited by network mesh size at long times

Prevent Membrane Sealing

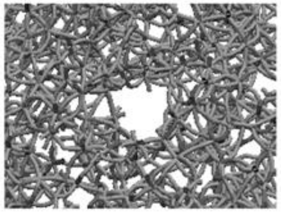
- **Introduce long rigid microrods in capsule interior**

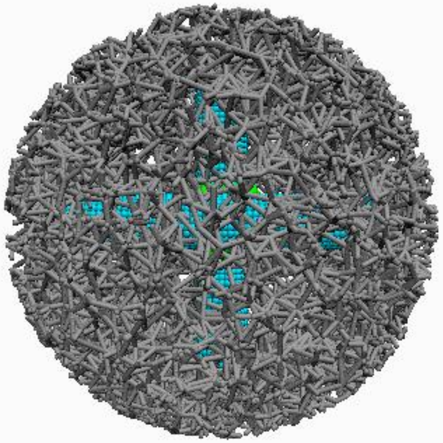


Deswelling



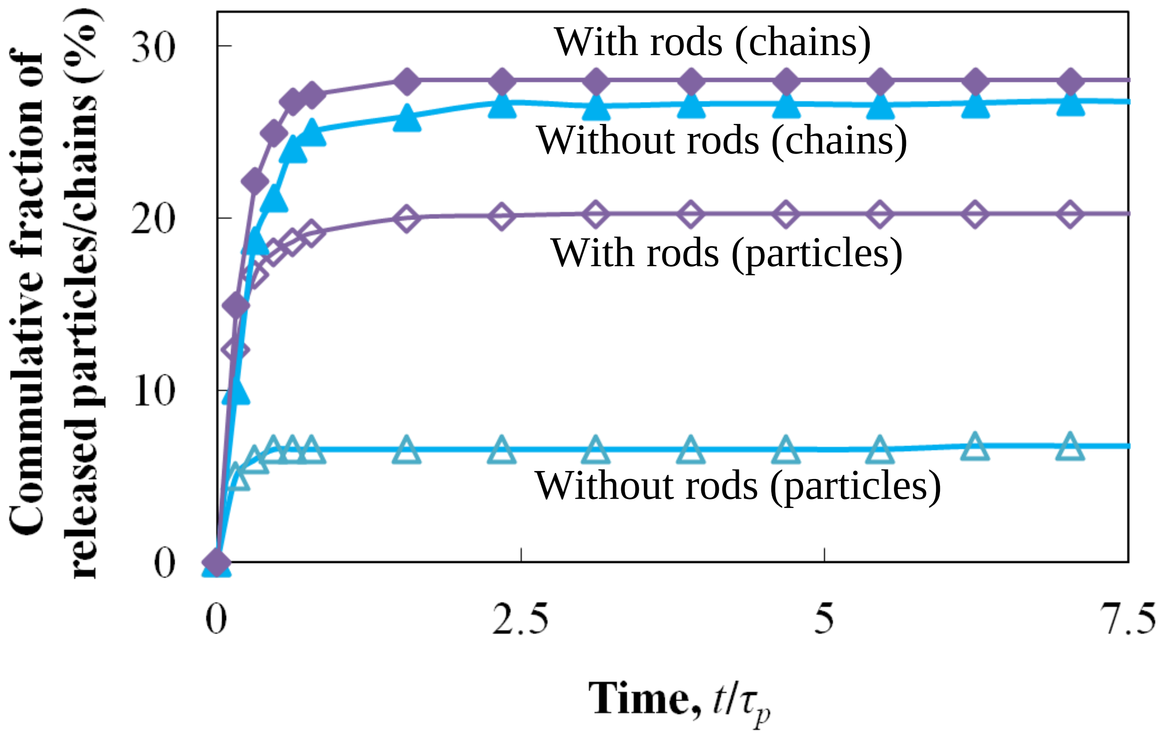
Deswelling
with
microrods





- **Rods stretch membrane of deswelling capsule and prevent pore closing**
  - ☞ Enhances flow driven release

Release From Deswelling Capsules With Rods



- **Inclusion of rigid microrods enhances nanoparticle release**
  - Membrane stretches due to interaction with rods
    - Mitigates rapid closure of membrane local “defects”
  - Chain release remains unaffected
    - Release of linear macromolecules is not limited by pore sealing

Scaling Analysis

- **Estimate rate of release during deswelling**
  - ☞ Compare relative strength of advective and diffusive transport

$$\mathrm{Pe} = \frac{\text{Rate of advective transport}}{\text{Rate of diffusive transport}} = \frac{ub}{D_{pn}}$$

$b = \text{Capsule wall thickness}$

$u = \text{Average discharge velocity} = \frac{\text{Rate of change of volume}}{\text{Surface area}} = \frac{\Delta V/\tau_c}{S}$

$D_{pn} = \text{Effective diffusion coefficient through capsule membrane}$

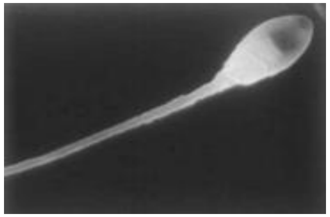
$\tau_c = \frac{R^2}{D_0} = \text{Time scale of capsule deswelling}$ $R = \text{Capsule outer radius at equilibrium}$

- **Good agreement with simulations of polymer chain release**
  - ☞ Model Pe = 450, simulations Pe = 420,
- **Qualitative agreement for nanoparticles**
  - ☞ Particle filtering due to decrease in membrane pore size
  - ☞ Good agreement with rods: model Pe = 120, simulations Pe = 90
    - ☞ Rods prevent particle filtering

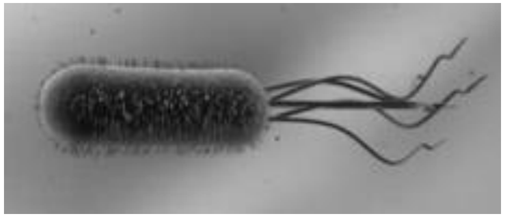
Microswimmers

- **Microswimmers – autonomous micro-scale vehicles that can self-propel in a fluid**
- **Numerous applications in nanotechnology, MEMS research, and medicine**
  - Drug delivery
  - Lab-on-a-chip applications
  - Micro-fabrication
- **Complex design of microswimmers limits their utilization**
- **Goal: design a simple and controllable microswimmer**
  - Utilize responsive hydrogel to drive microswimmer

Natural microswimmers

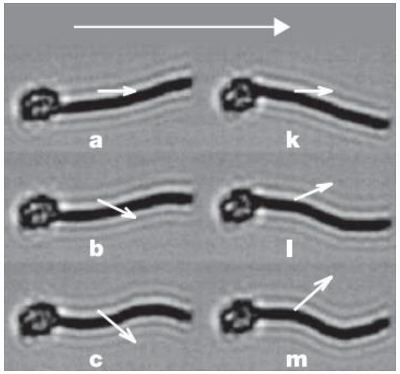


Spermatozoid

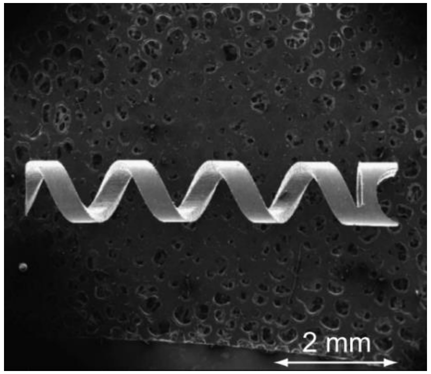


E.Coli

Artificial microswimmers

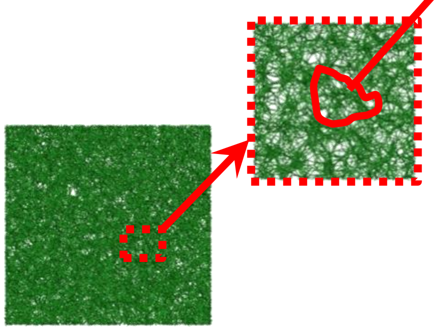


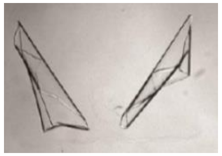
Dreyfus, *Nature*, 2005



Tiantian, *HAL*, 2014

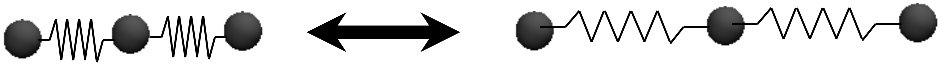
Bi-layered Gel

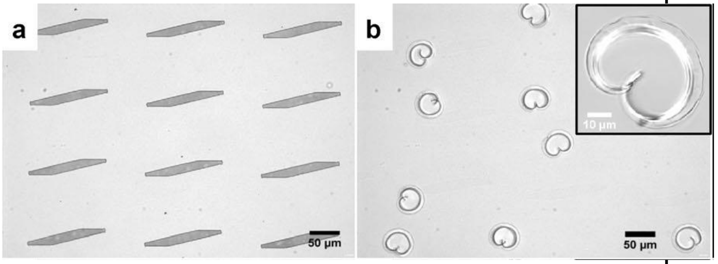




Ionov, *ACS Nano*, 2012

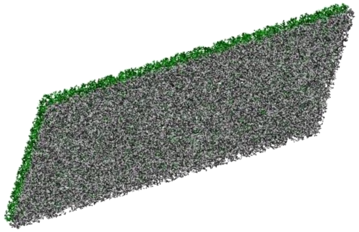
- **Gel modeled as random network of interconnected elastic filaments (springs)**
  - Filaments composed of stretching and bending springs connecting DPD beads
  - Networks is immersed in DPD solvent
- **Gel volume transition is modeled by varying equilibrium length of network filaments**
  - Accounts for internal stresses that cause network to shrink or expand

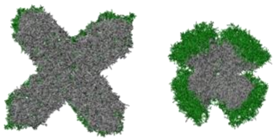




Ye et al, *Angew Chem*, 2015

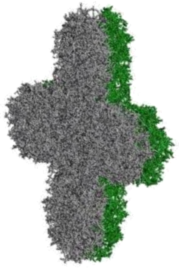
- **Swelling bi-layered sheets undergo bending**
  - Sheets have identical material properties
  - One layer expands in response to stimulus
  - Second layer is passive

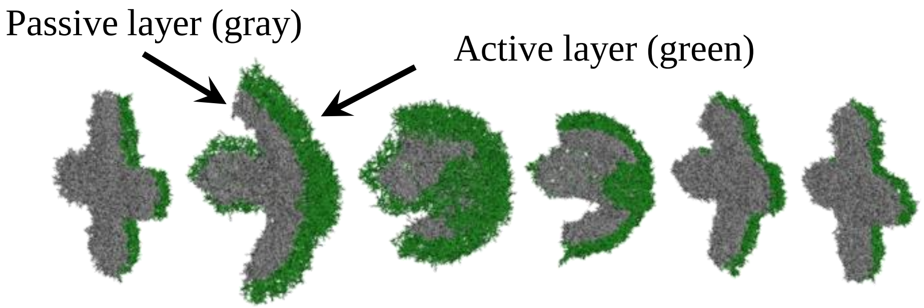


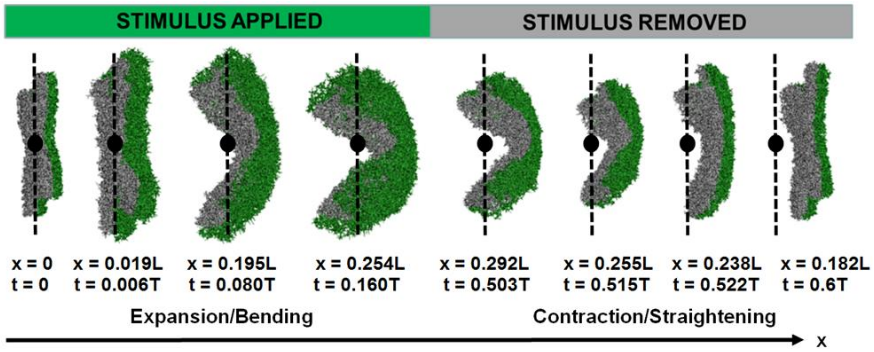


Gel Microswimmer

- **Bi-layered gel deforms upon periodic stimulus application**
  - Mismatch between stresses at gel interface
  - Internal bending moment in network develops
- **X-shaped geometry**
  - Large arms maximize bending
- **Swimming process 4 steps:**
  - Expansion
  - Bending
  - Contraction
  - Straightening
- **Each periodic application of stimulus produces net forward displacement**



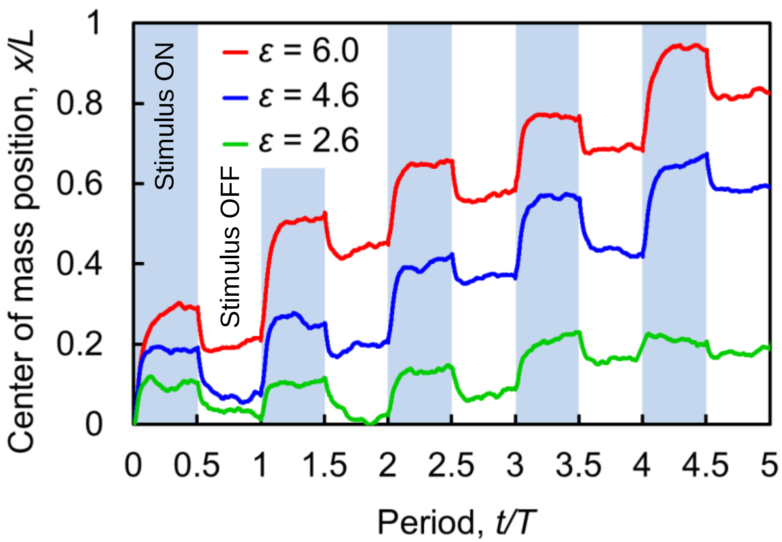


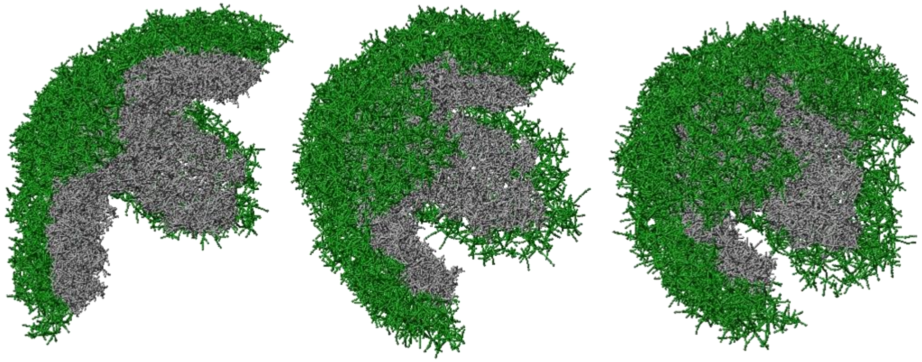


Swimming Cycle

- **Swimmer trajectory**
  - Large forward displacement during expansion and bending phases
  - Small backward displacement during contraction and straightening phases
- **Swimmer speed similar to that of *E.coli***
  - ~ 0.2 body-lengths/period
- **Larger ε leads to better swimming performance**

$$\varepsilon = \frac{\text{expanded network volume}}{\text{contracted network volume}}$$



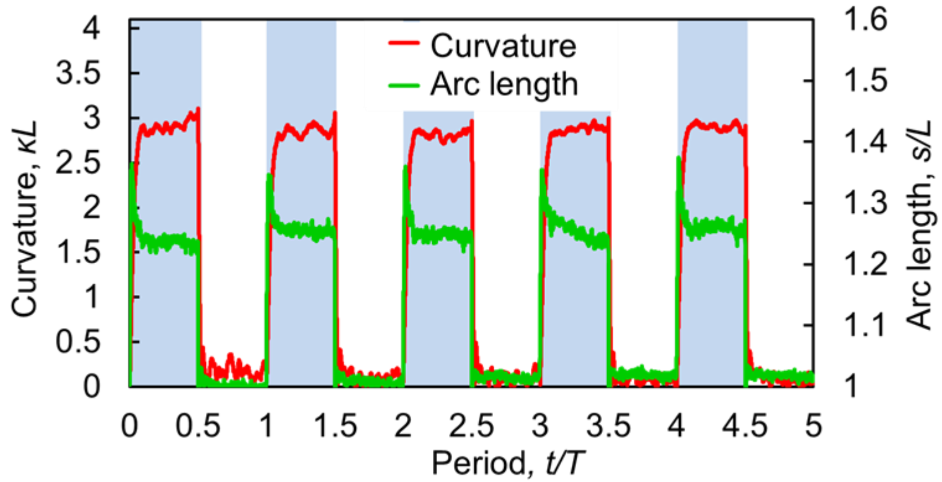


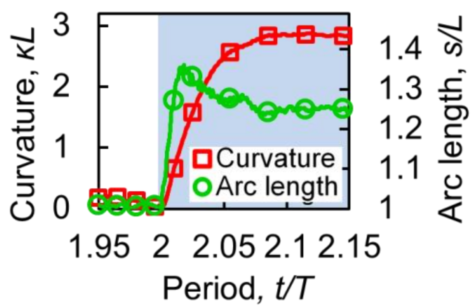
$\varepsilon = 2.6$ $\varepsilon = 4.6$ $\varepsilon = 6.0$

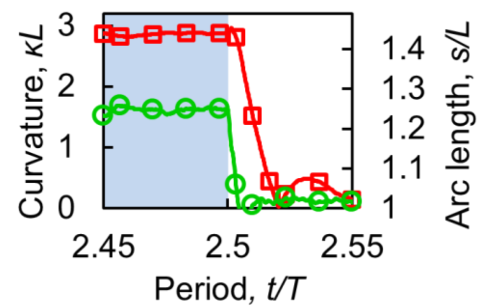
Geometric configurations at $t / T = 0.5$

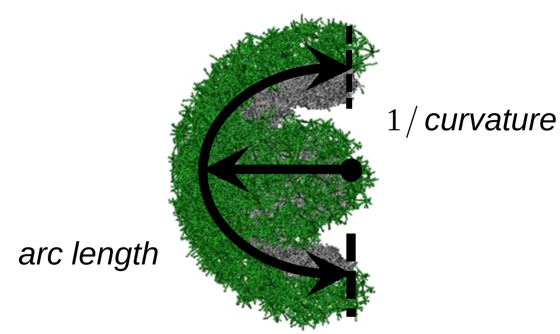
Why swimmer swims at low Reynolds number

- ❑ **Need to create time irreversible motion**
- ❑ **Characterize swimmer kinematics**
  - ☞ Arc length (extension)
  - ☞ Curvature (bending)
- ❑ **Hydrodynamic drag for bending is larger than drag for extension**
  - ☞ Leads to time delay between changes in arc length and curvature
- ❑ **Swimmer propels due to timescale difference between bending/expansion**





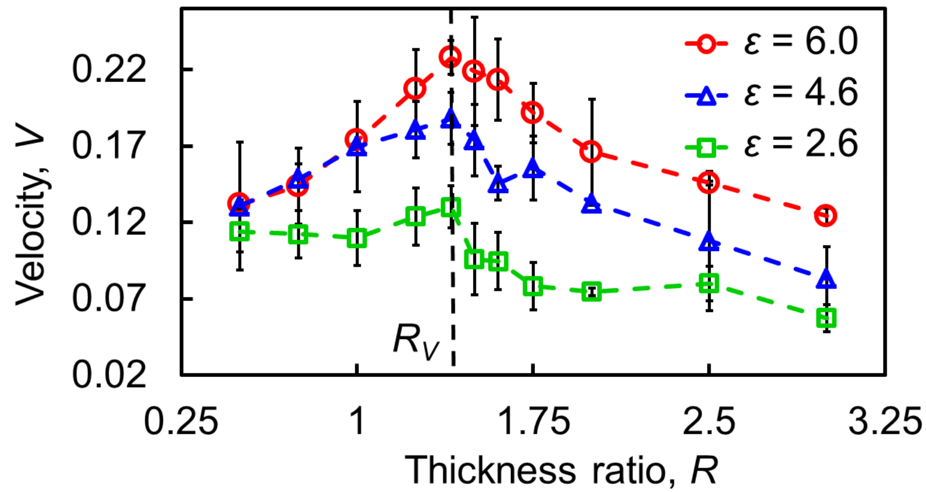


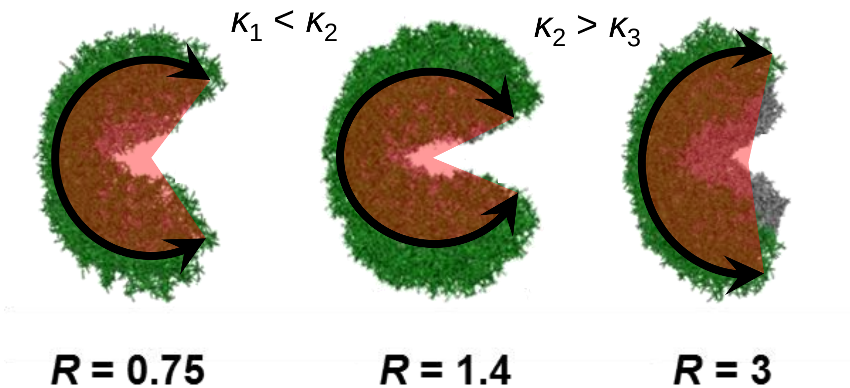


Optimizing Swimming Performance

$$R = \frac{\text{passive layer thickness}}{\text{active layer thickness}}$$

- **Swimming performance defined by**
  - Swelling ratio (ε)
  - Relative elasticity (thickness) of sheets (R)
- **Larger swelling ratios lead to faster propulsion**
- **Gel thickness ratio defines swimmer bending**
  - Passive layers that are either too thick or too thin hinder bending
- **Best swimming performance occurs for a thickness ratio of 1.4**

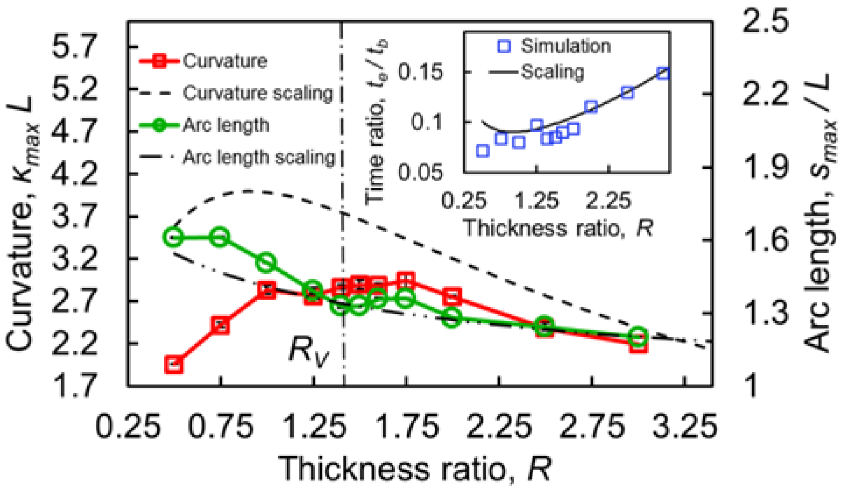




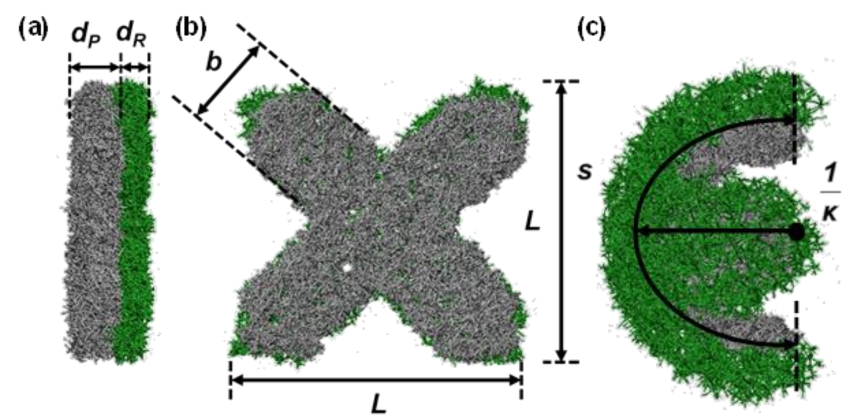
Scaling Analysis

- **Increasing *R* leads to a monotonic decrease in swimmer's extension**
  - ☞ $L_s/L \sim \left(\varepsilon^{1/3}+R\right)/\left(1+R\right)$, ($L_s$ is swollen length)
- **For low/high *R* values curvature decreases**
  - ☞ Leads to poor swimming performance
  - ☞ $\kappa L \sim \dfrac{6R\left(1-\varepsilon^{-1/3}\right)}{\varepsilon^{1/3}\left(1+R\varepsilon^{-1/3}\right)^3}\left(\dfrac{L}{d_R}\right)$

  where κ is the curvature

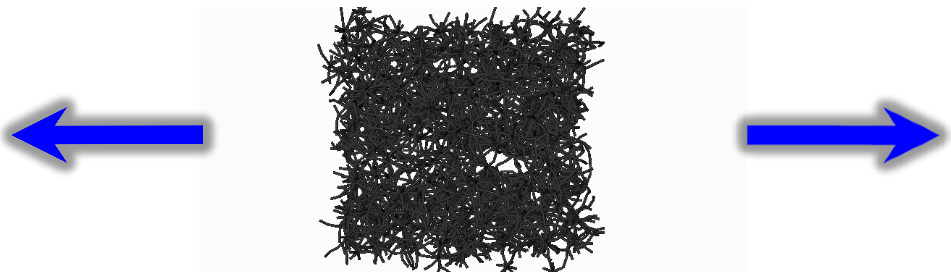


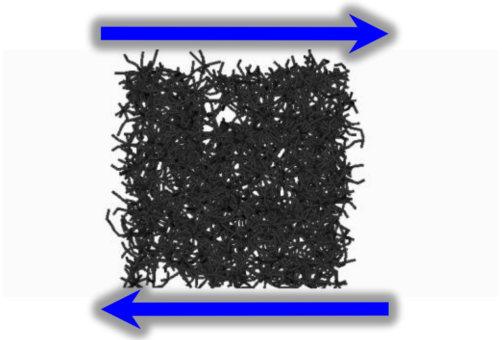
- **The ratio of extensional and bending time scales**
  - ☞ $\dfrac{t_e}{t_b} \sim \dfrac{C_e}{C_b}\dfrac{8\left(1+R\varepsilon^{-1/3}\right)^3}{3R\varepsilon^{-1/3}}\left(\dfrac{d_R}{L}\right)^2$
  - ☞ $C_e/C_b \sim 0.5$ is ratio of drag coefficients for extension and bending
  - ☞ Theory predicts t_e/t_b minimum at $R \sim 1$
- **Theory supports computational models**



Summary: Polymer Network

- ❑ **Developed mesoscale model for random polymer networks**
  - ☞ Validated by simulating transport properties and swelling kinetics
    - ☞ Good agreement with theory and experiment
- ❑ **Examined transport in mechanically deformed (anisotropic) networks**
  - ☞ Stretching enhances permeation and diffusion in direction of deformation
  - ☞ Total diffusivity remains unchanged under deformation
  - ☞ Permeability defined by internal network orientation

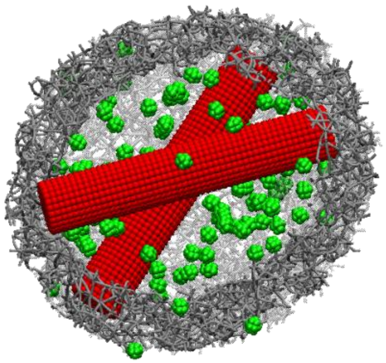




Masoud and Alexeev, Permeability and diffusion through mechanically
deformed random polymer networks ***Macromolecules*** 43, 10117 (2010)

Summary: Microgel Capsules

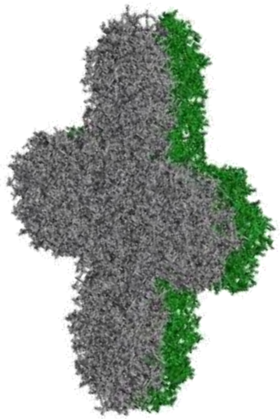
- **Responsive capsules enable control over release dynamics**
  - ☞ Swollen microgel capsules: slow diffusive release
  - ☞ Deswelling capsules: fast hydrodynamic release
    - ☞ Precise control over released amount
    - ☞ Pulsatile release with repeating stimuli
- **Applications**
  - ☞ Targeted drug delivery, in-vivo sampling, viruses removal, detoxification



Masoud and Alexeev, Controlled release of nanoparticles and macromolecules from responsive microgel capsules ***ACS Nano*** 6, 212, 2012

Summary: Gel Swimmer

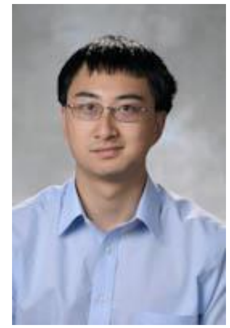
- **Designed a simple self propelling hydrogel microswimmer**
- **Examined effects of swelling ratio**
  - ☞ Larger ratios lead to faster swimming
- **Developed an approach for optimizing swimming performance**
  - ☞ $R \sim 1.4$ improves swimming speeds
- **Explained fundamentals behind time irreversible motion**
  - ☞ Time delay between expansion and bending

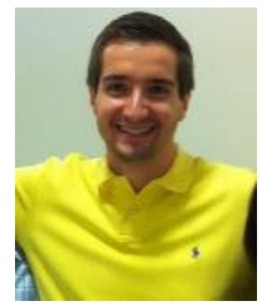


Nikolov, Yeh, Alexeev, Self-propelled microswimmer actuated by stimuli-sensitive bilayered hydrogel. ***ACS Macro Letters*** 4, 84, 2015.

Acknowledgment

- **Students:**
  - ☞ Hassan Masoud
  - ☞ Peter Yeh
  - ☞ Svetoslav Nikolov





- **Funding:**
  - ☞ ACS-PRF Doctoral New Investigator Award
  - ☞ NSF CAREER Award (DMR-1255288)