Ordering and instabilities in dense bacterial populations

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UCSD

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UNAM, Mexico

Bacteria are everywhere

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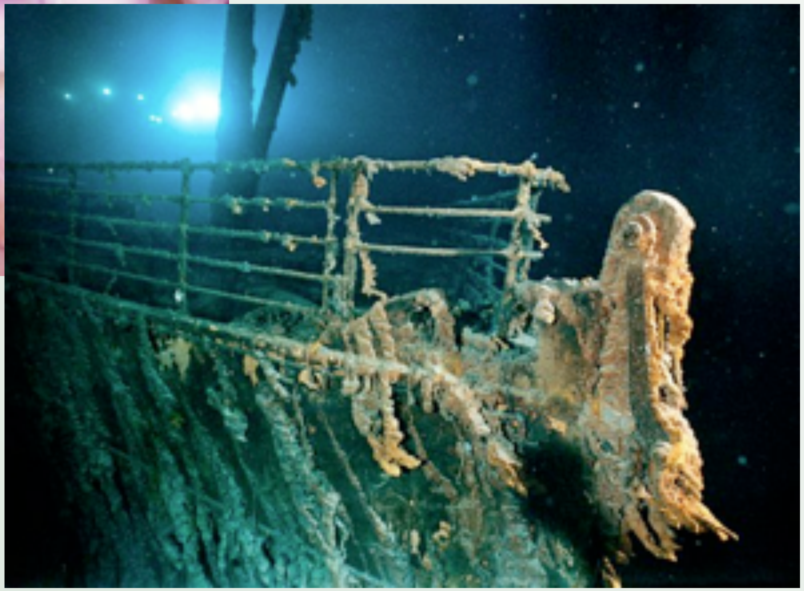
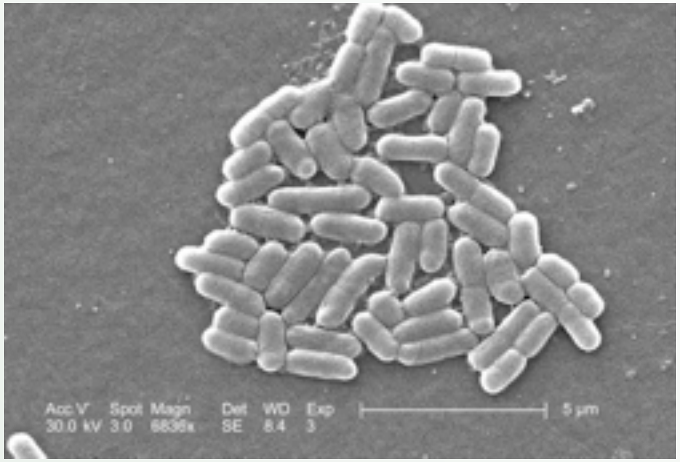


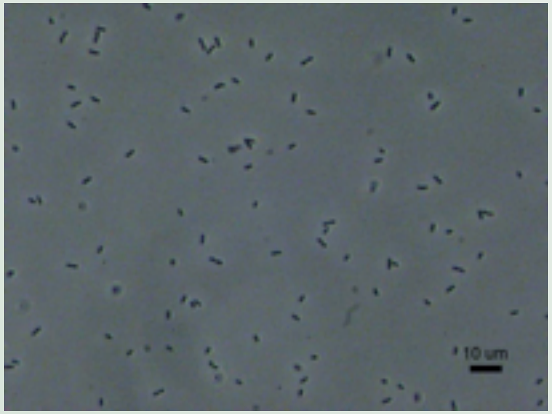
Bacteria are everywhere

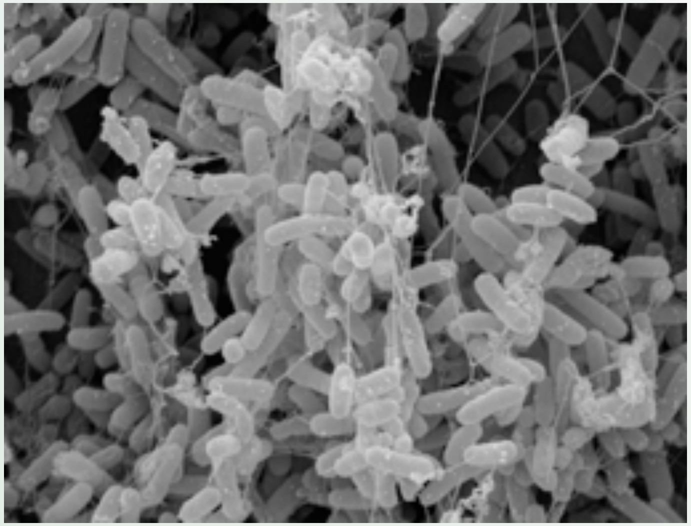
Bacteria are everywhere

- 10^7-10^9 species
- 90,000 species of bacteria in human gut
- 10x more cells in human body than human cells
- bacterial biomass: $5 \cdot 10^{11}$ ton;
  10x biomass of all animals and plants
- overall on Earth: ~10^{30} cells

E.coli biofilms

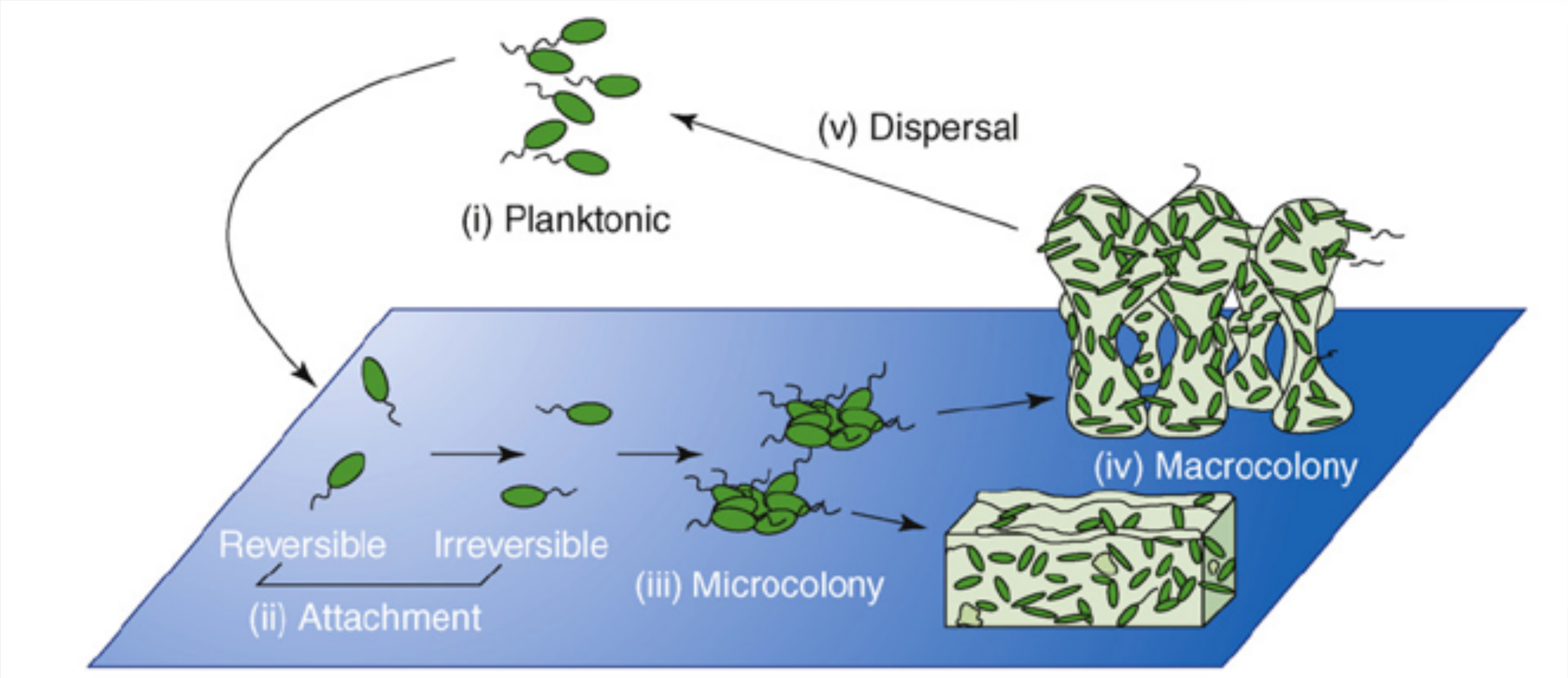






Biofilms

Developmental cycle of biofilm formation



(Monds and O'Toole, 2009)

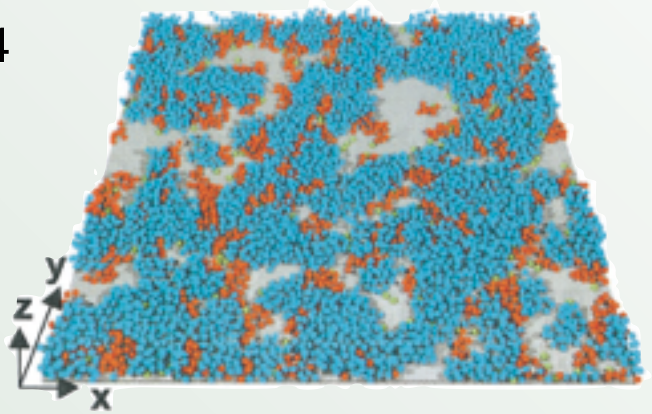
Important factors:

- motility/chemotaxis
- adhesion
- extracellular matrix (EPS)
- cell-cell communication/cooperation
- gene regulation/adaptation
- mechanical stresses/flows

Modeling of biofilm formation

- ODE/PDE mass transport and biochemical reactions models:
  - reaction/diffusion for biomass and substrates
  - fluid dynamics for the liquid flow
  - structural mechanics for biofilm growth and EPS
  - AQUASIM; Wanner & Reichert, 1996

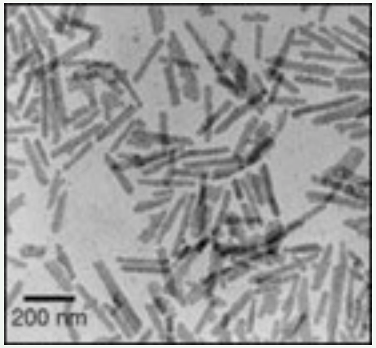
- Discrete-element models
  - cellular automata (rule-based); Wimpenny & Colasanti, 1997
  - individual cells; BacSim, Kreft et al, 1998
  - biomass "particles"; Picioreanu et al, 2004



Granular rods at different scales

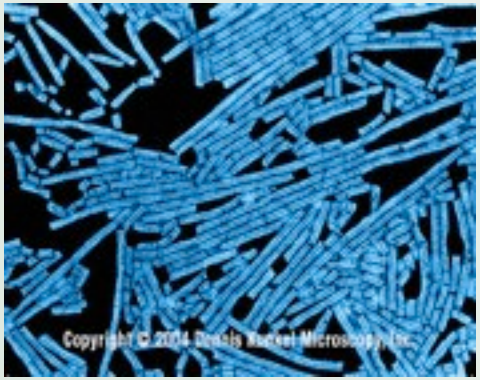
- Industrial applications

- Colloids and nano-particles



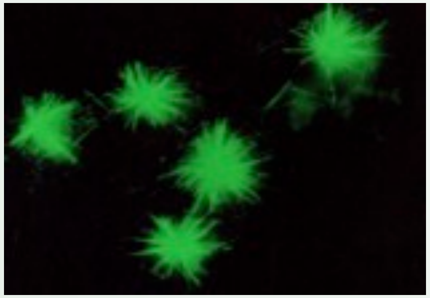
- Bacteria and viruses

E.coli



Tobacco mosaic virus

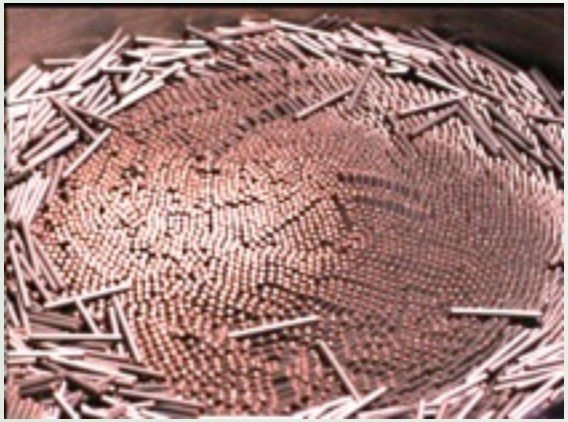
- Biomolecules



microtubules

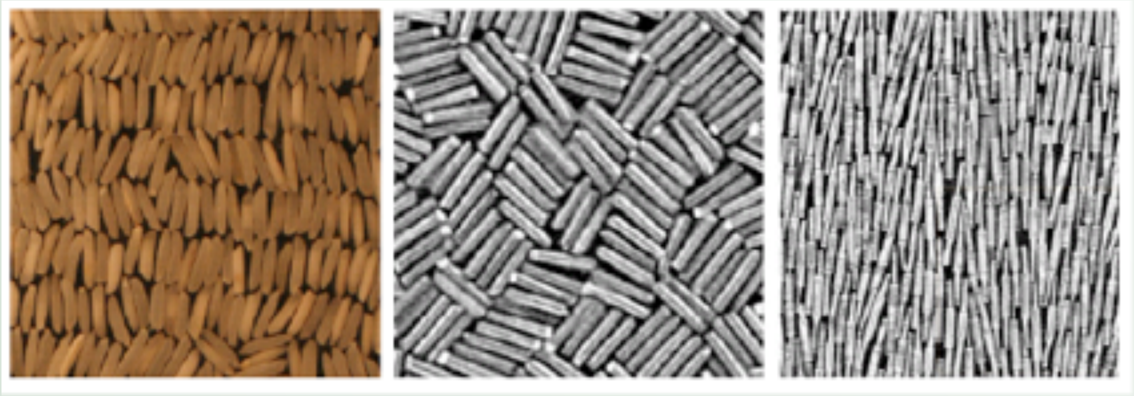
Ordering of vibrated granular rods

Blair, Neicu, Kudrolli, 2003



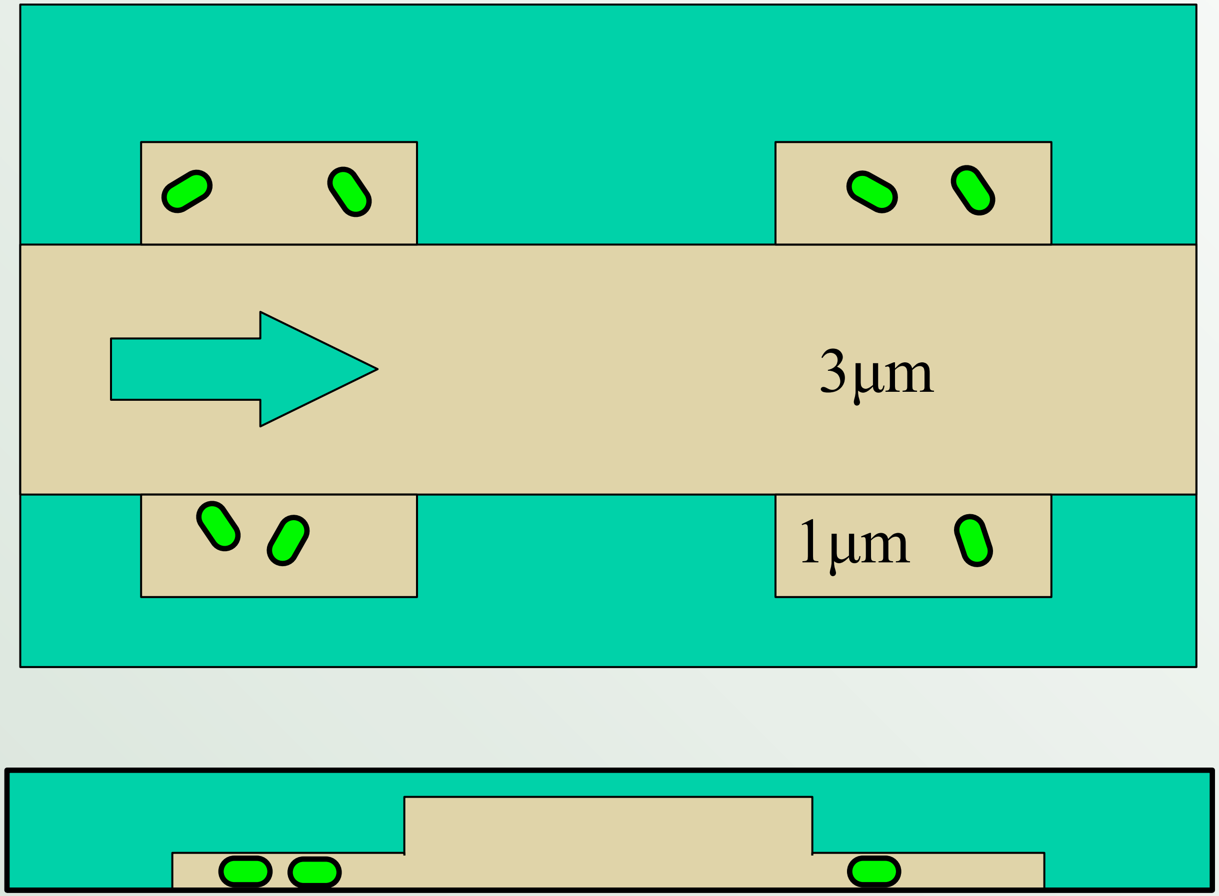
Vertical alignment
(1-layer smectic)

Narayan, Menon, Ramaswamy, 2006



smectic tetratic nematic

a typical microfluidic setup



A typical experiment

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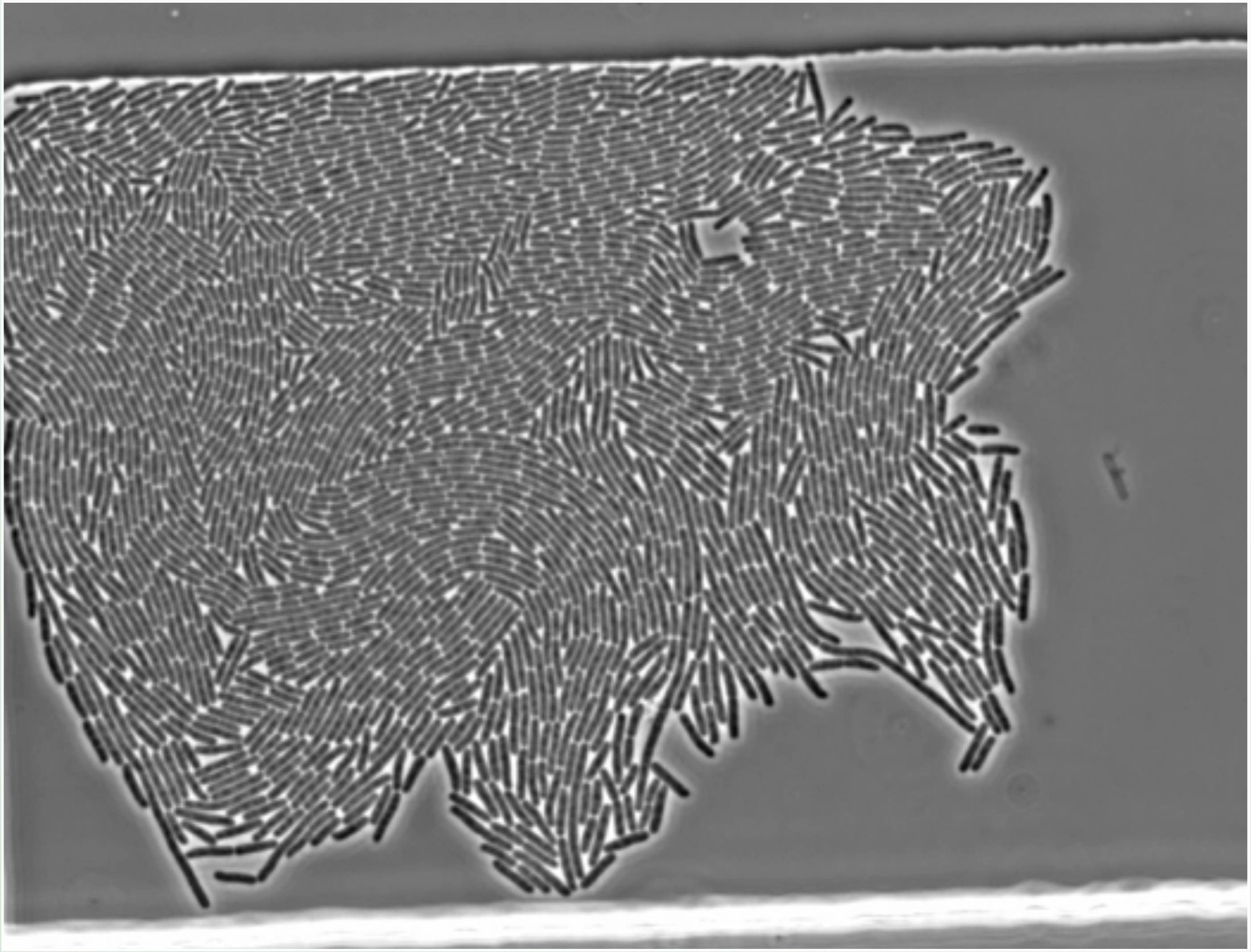
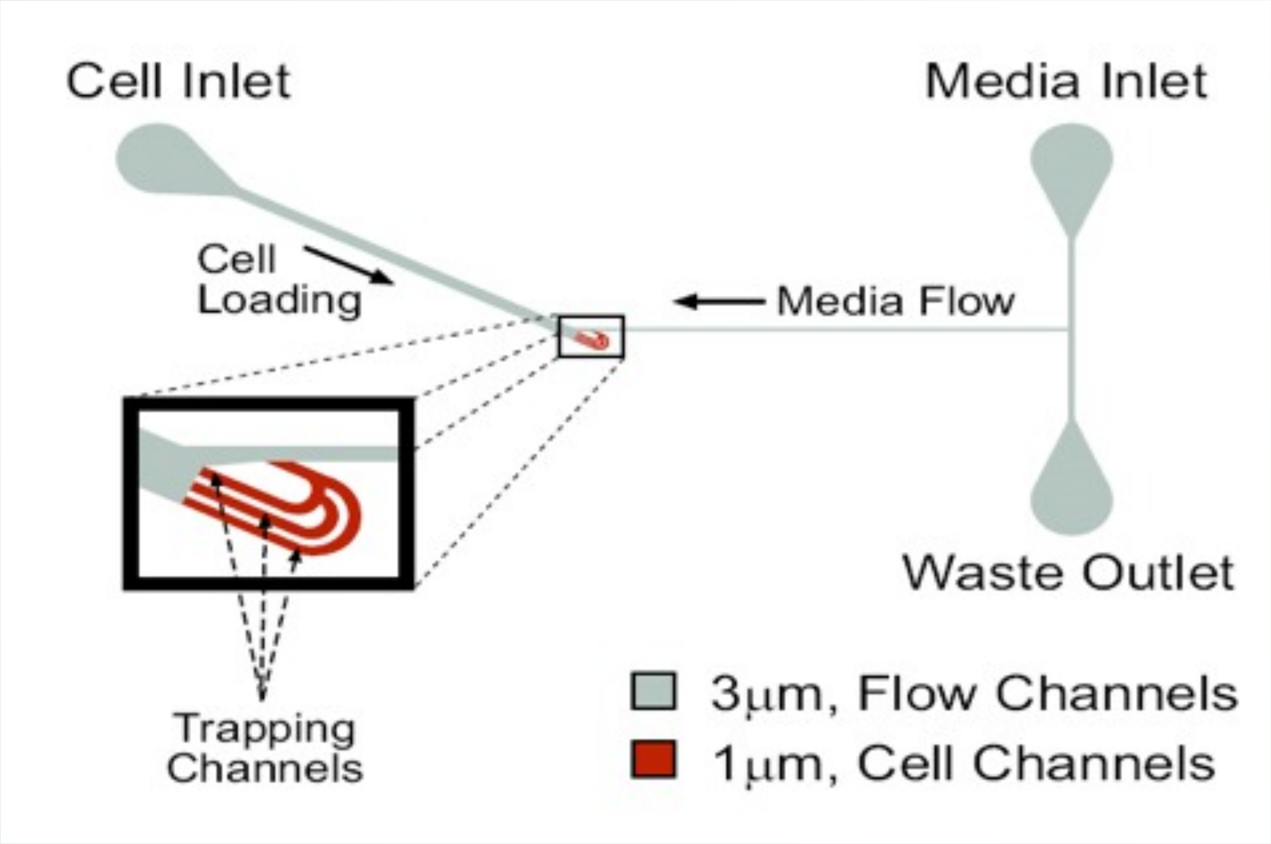


Local nematic order is spontaneously formed... Mechanism?

Microfluidic Tesla device



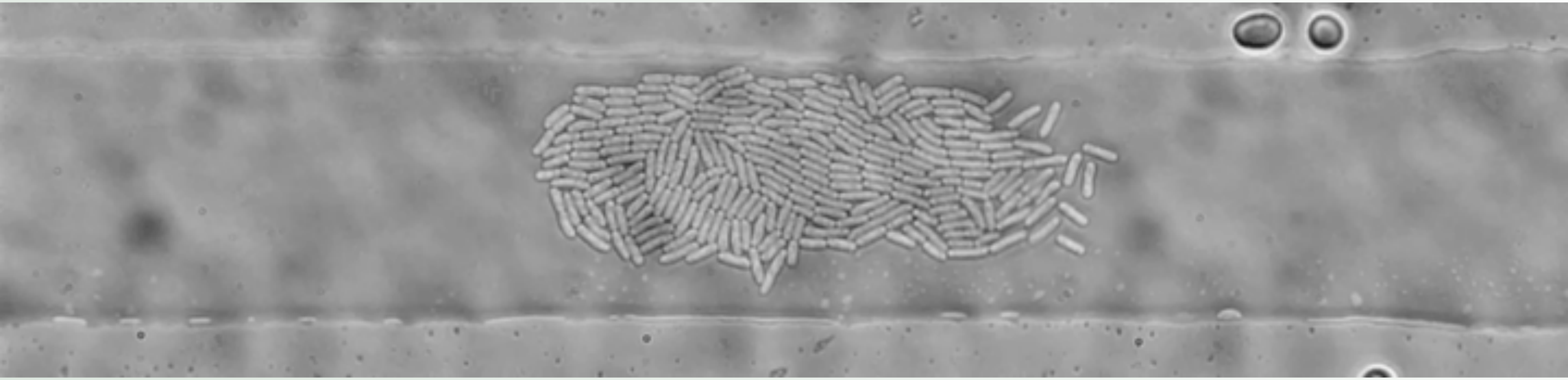
Experiments in an open channel

localized

uniform

Experiments in an open channel

localized



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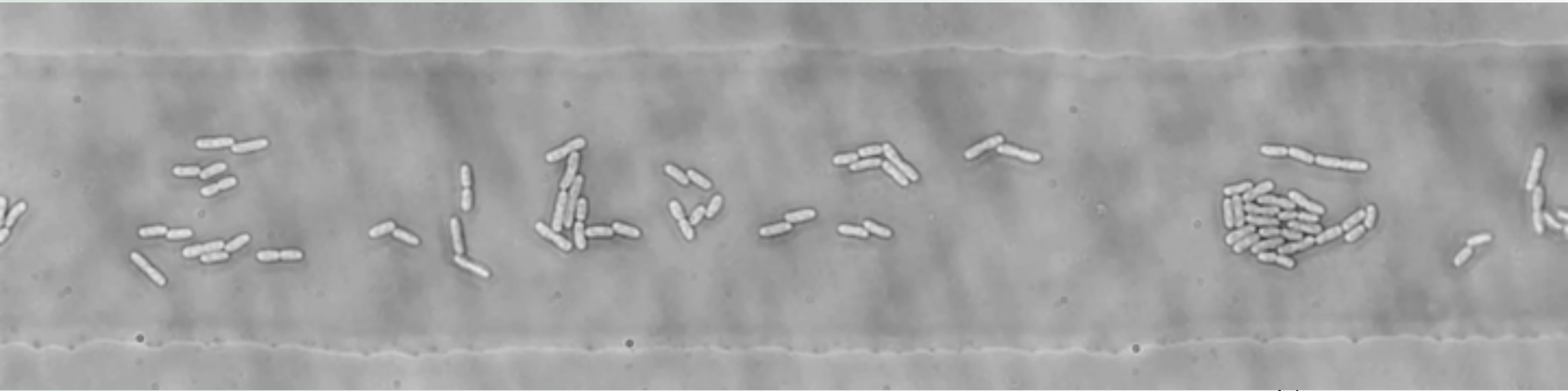

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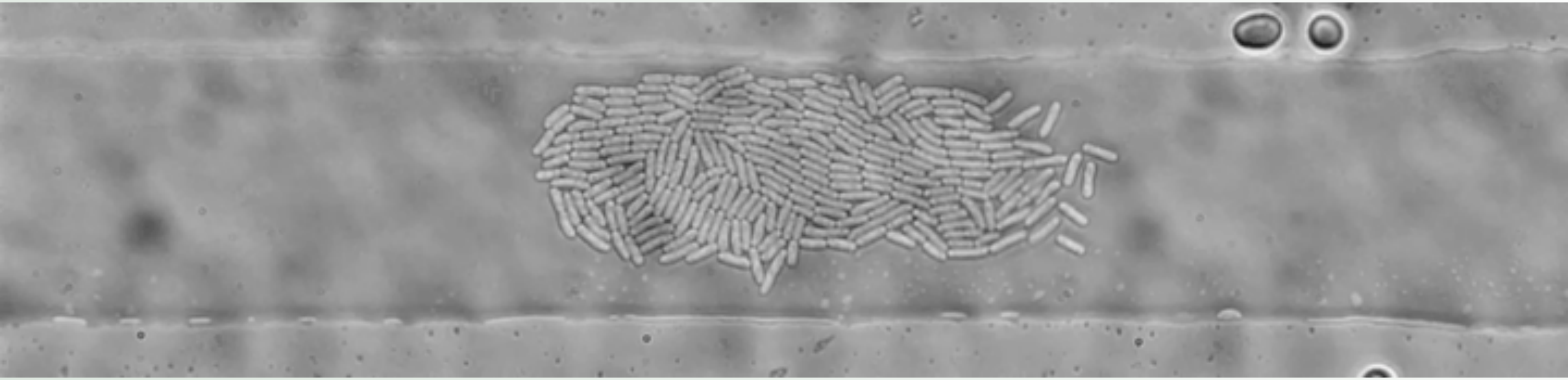

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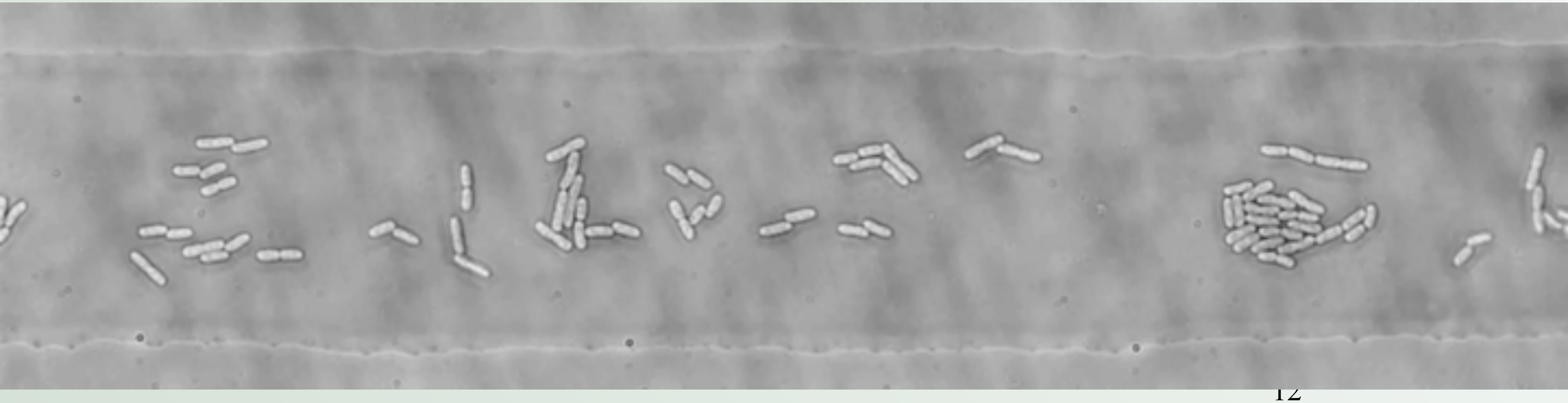
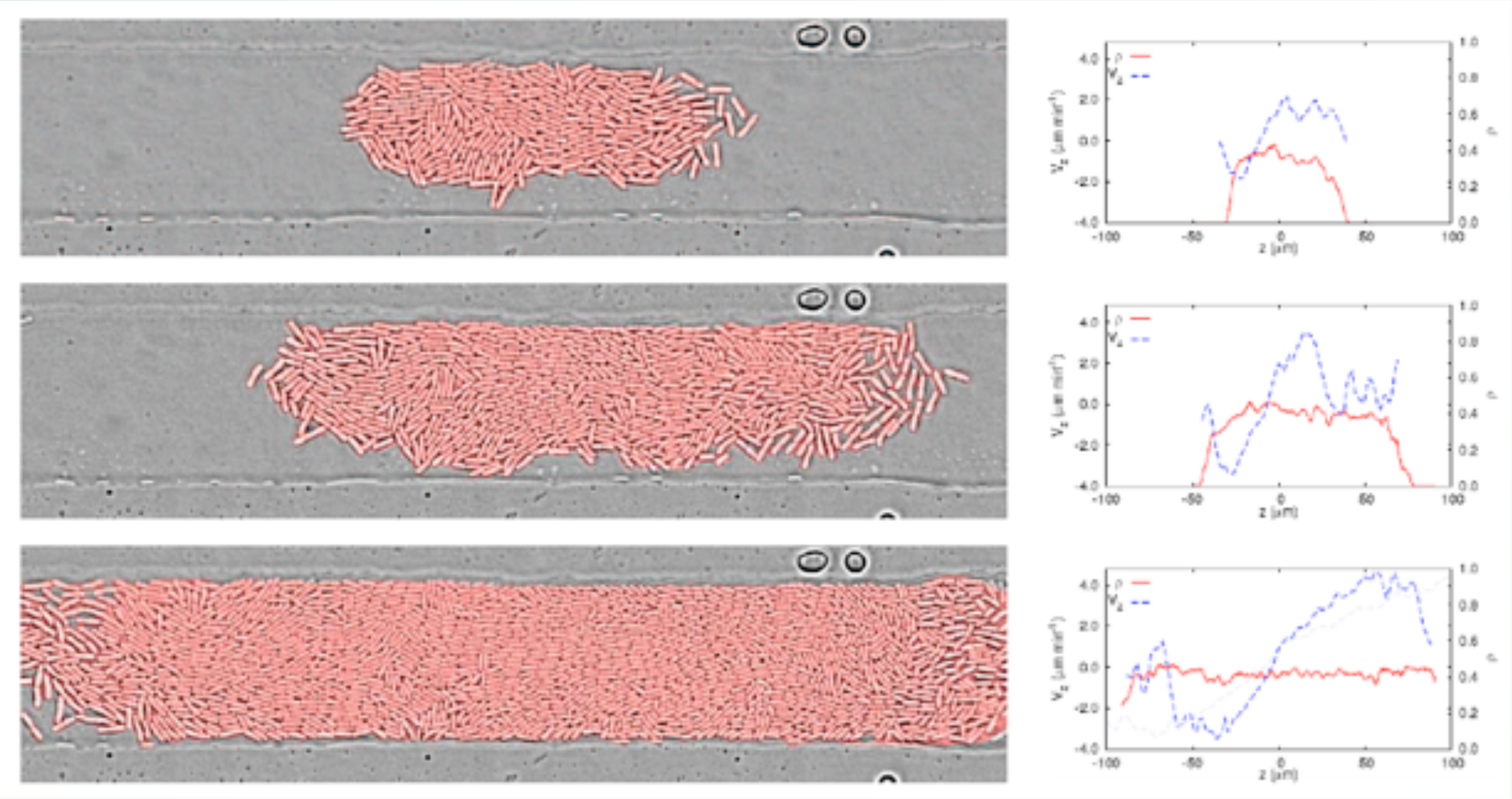
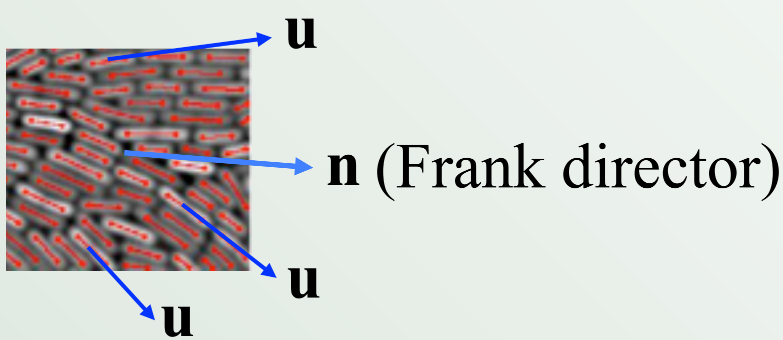


Data processing (PIV)

localized



Nematic order parameter

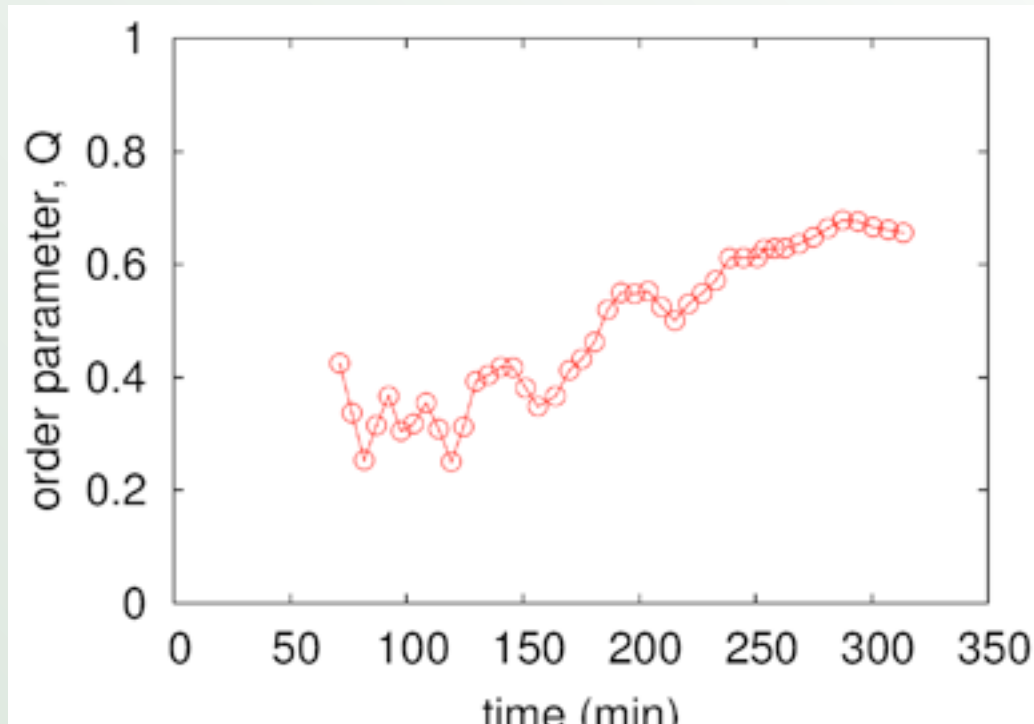


$$Q_{ij} = \langle u_i u_j - d^{-1}\delta_{ij} \rangle$$

$$Q_{ij} = 2Q(n_i n_j - \frac{1}{2}\delta_{ij})$$

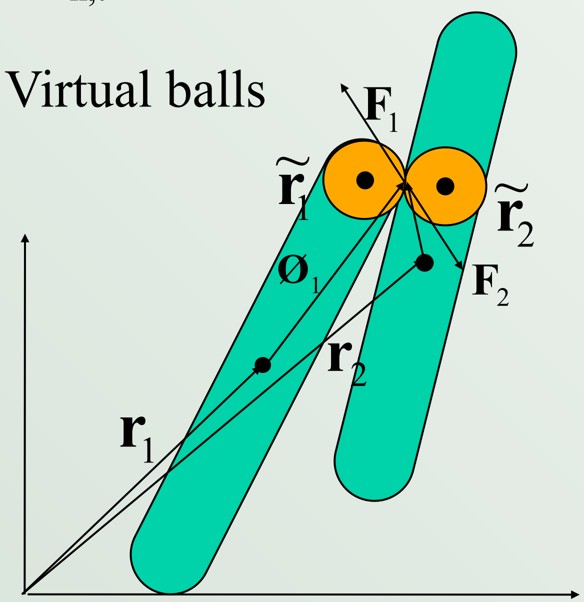
Magnitude

$$Q = [\langle \cos 2\phi \rangle^2 + \langle \sin 2\phi \rangle^2]^{1/2}$$



MD simulations

- γ_n normal damping
- μ friction
- $k_{n,t}$ spring constants



Contact forces

$$\mathbf{v}^{ij} = \mathbf{v}^i - \mathbf{v}^j + (R^i\omega^i + R^j\omega^j)\mathbf{t}^{ij}$$

$$v_n = (\mathbf{v}^i - \mathbf{v}^j)\mathbf{n}^{ij}, \qquad v_t = (\mathbf{v}^i - \mathbf{v}^j)\mathbf{t}^{ij} + (R^i\omega^i + R^j\omega^j)$$

$$\delta_n = R^i + R^j - |\mathbf{r}^i - \mathbf{r}^i| > 0$$

$$F_n = k_n\delta_n - 2\gamma_n m_e v_n$$

$$F_t = -\mathrm{sign}(\delta_t)\min(|k_t\delta_t|, |\mu_t F_n|), \qquad \delta_t(t) = \int_{t_0}^{t} v_t(\tau)\,d\tau$$

Newton equations

$$m^i \frac{d^2\mathbf{r}^i}{dt^2} = m^i\mathbf{g} + \sum_c \mathbf{F}^{ic},$$

$$I^i \frac{d\omega^i}{dt} = R^i \sum_c F_t^{ic},$$

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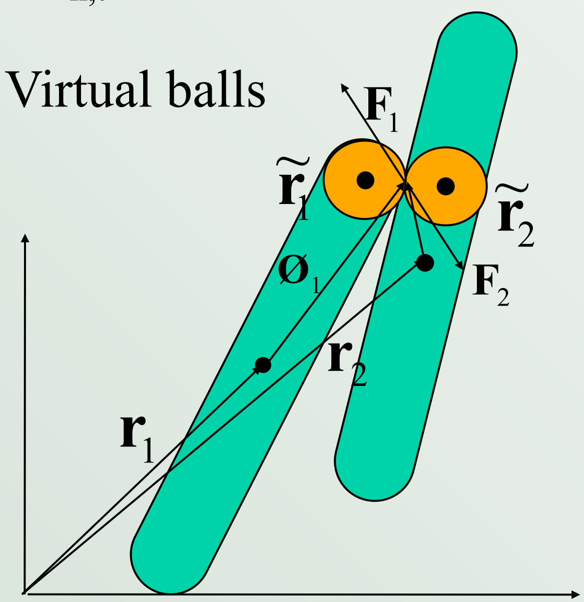

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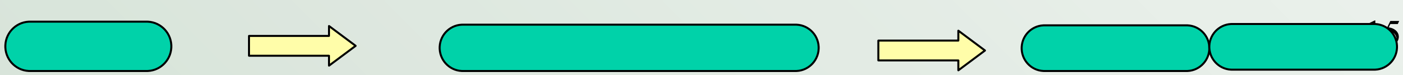
$$I^i\frac{d\omega^i}{dt} = R^i\sum_c F_t^{ic},$$

In addition to this, rods grow and divide:

$$l = l_0\exp[\alpha t], \text{ if } l > l_m \simeq 2l_0, \text{ divide}$$



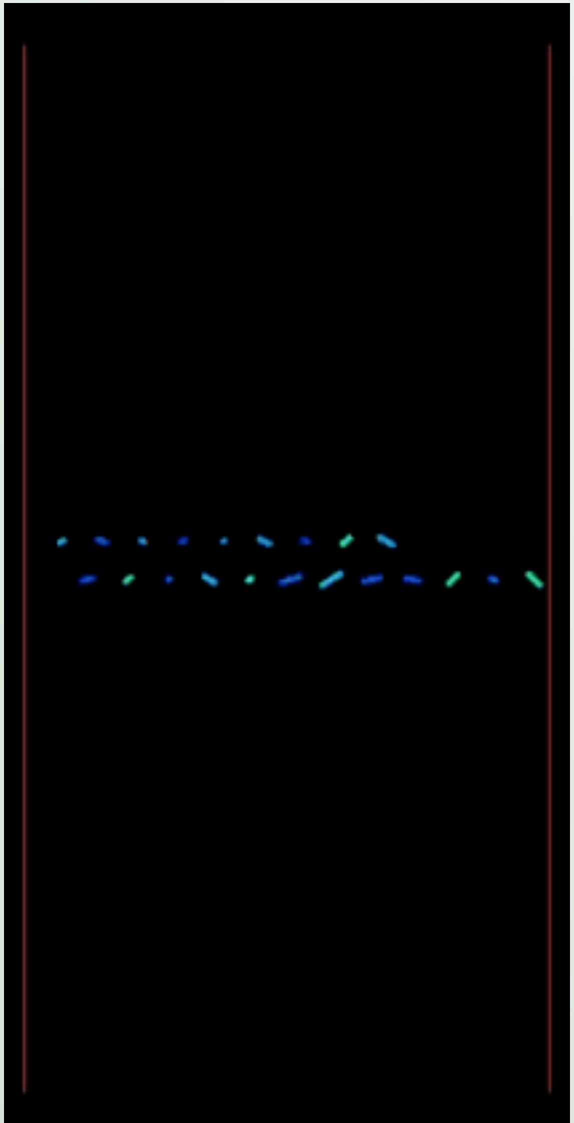
MD simulations

$82d \times 164d \times 1d$ open channel

Localized initial conditions

Pressure-independent growth

MD simulations

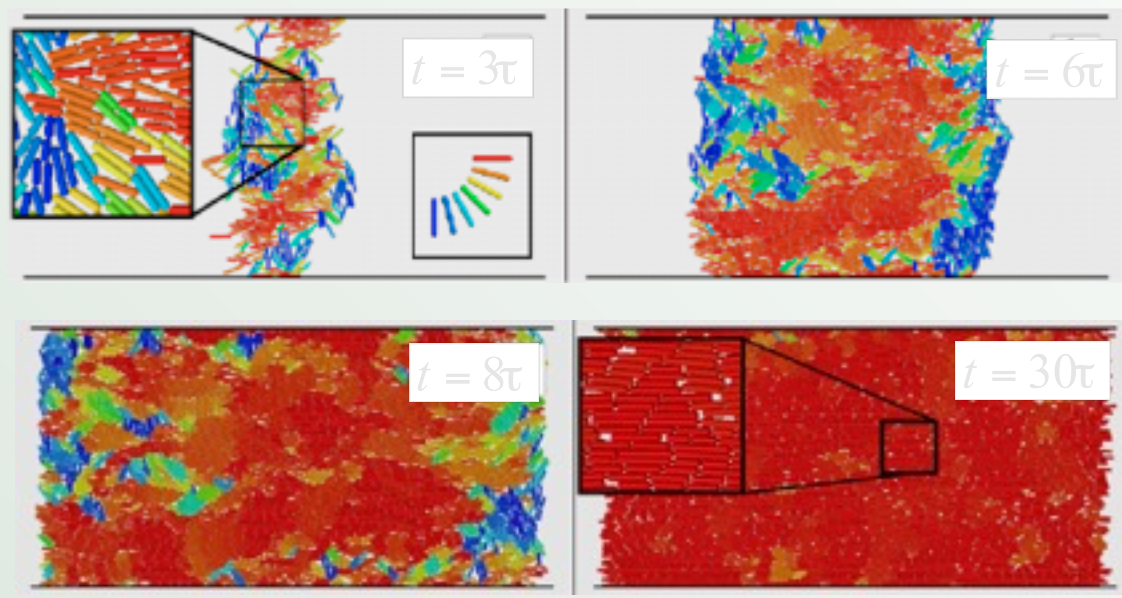


$82d \times 164d \times 1d$ open channel

Localized initial conditions

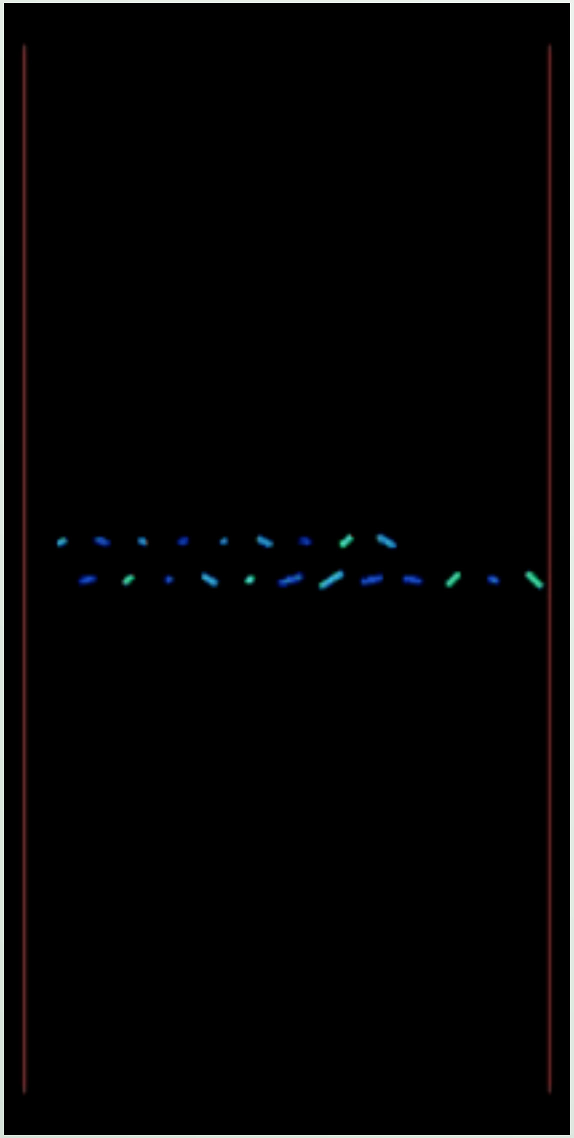
Pressure-independent growth

division time $\tau = 20\,\text{min}$



color: orientation

MD simulations



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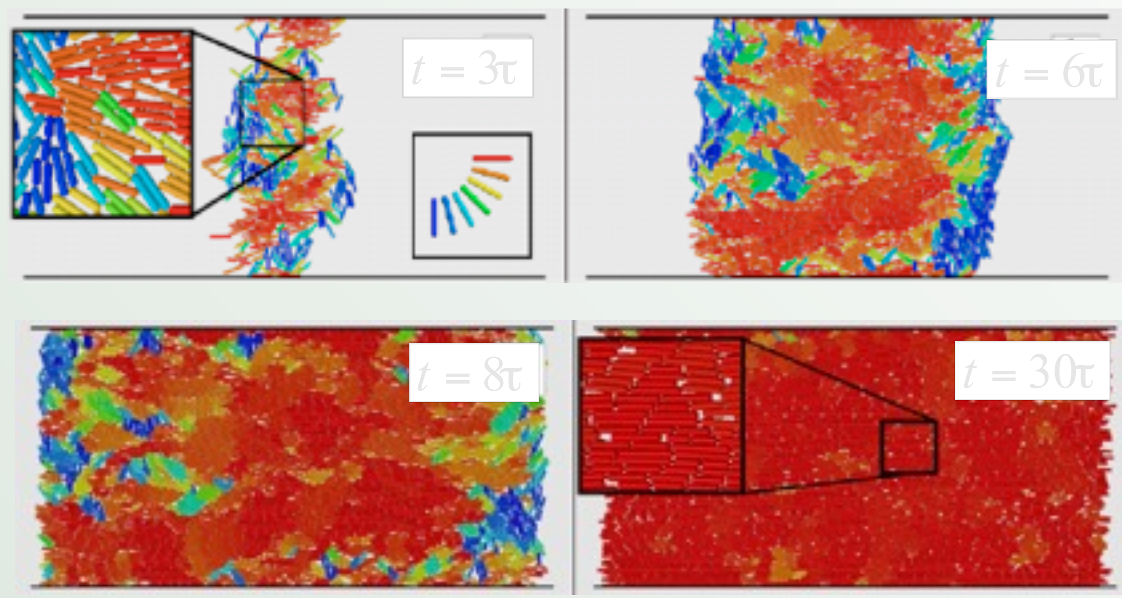

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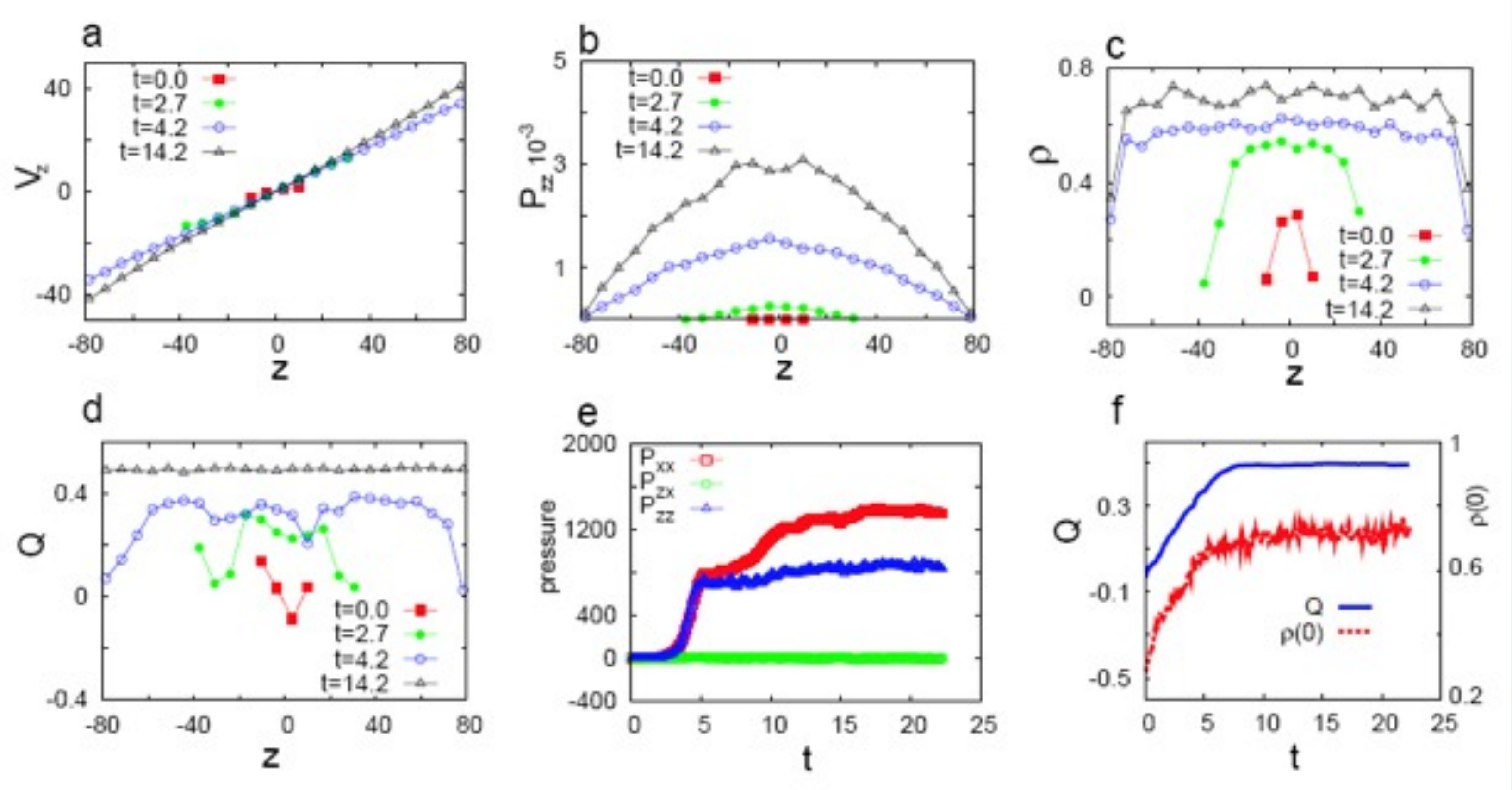
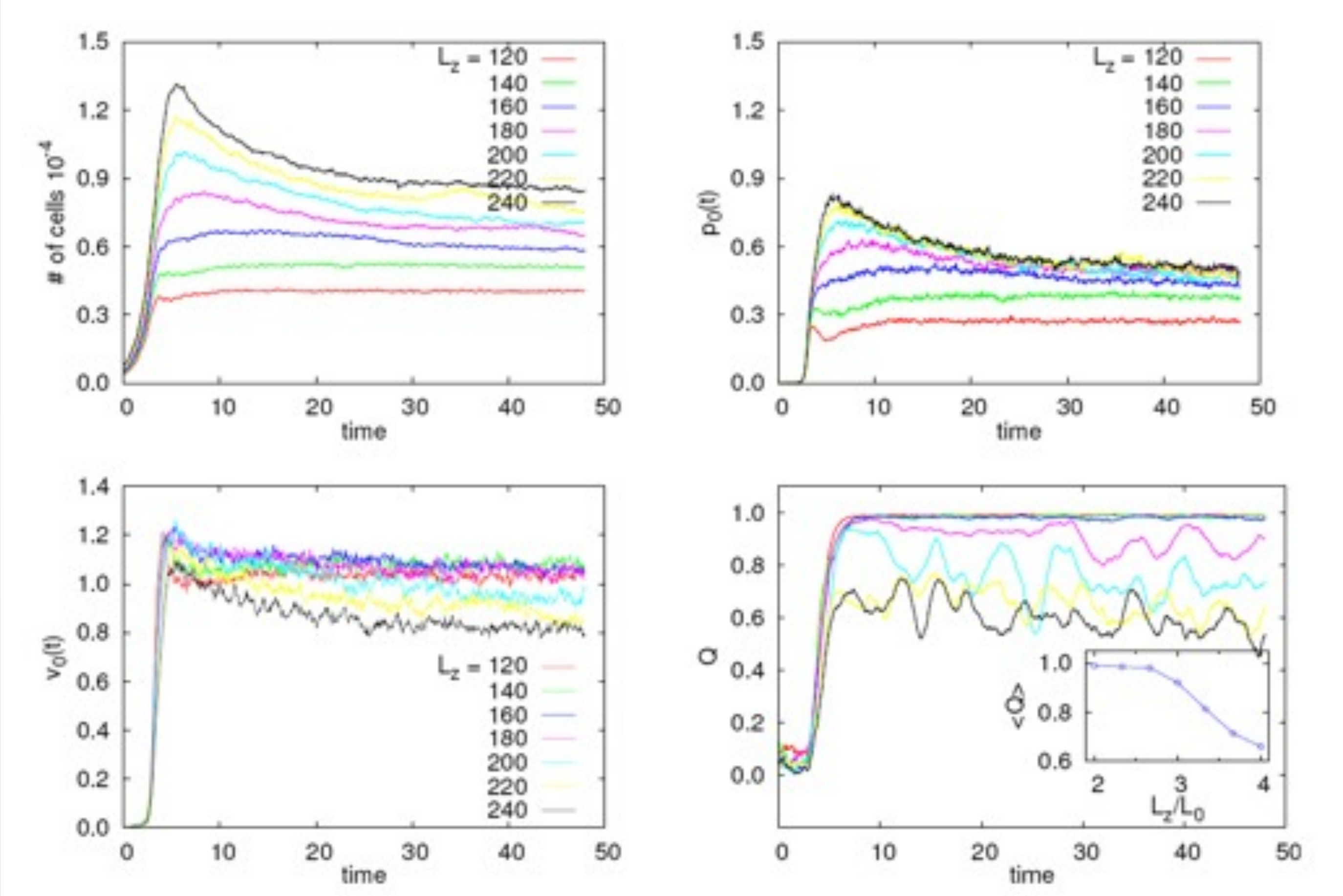


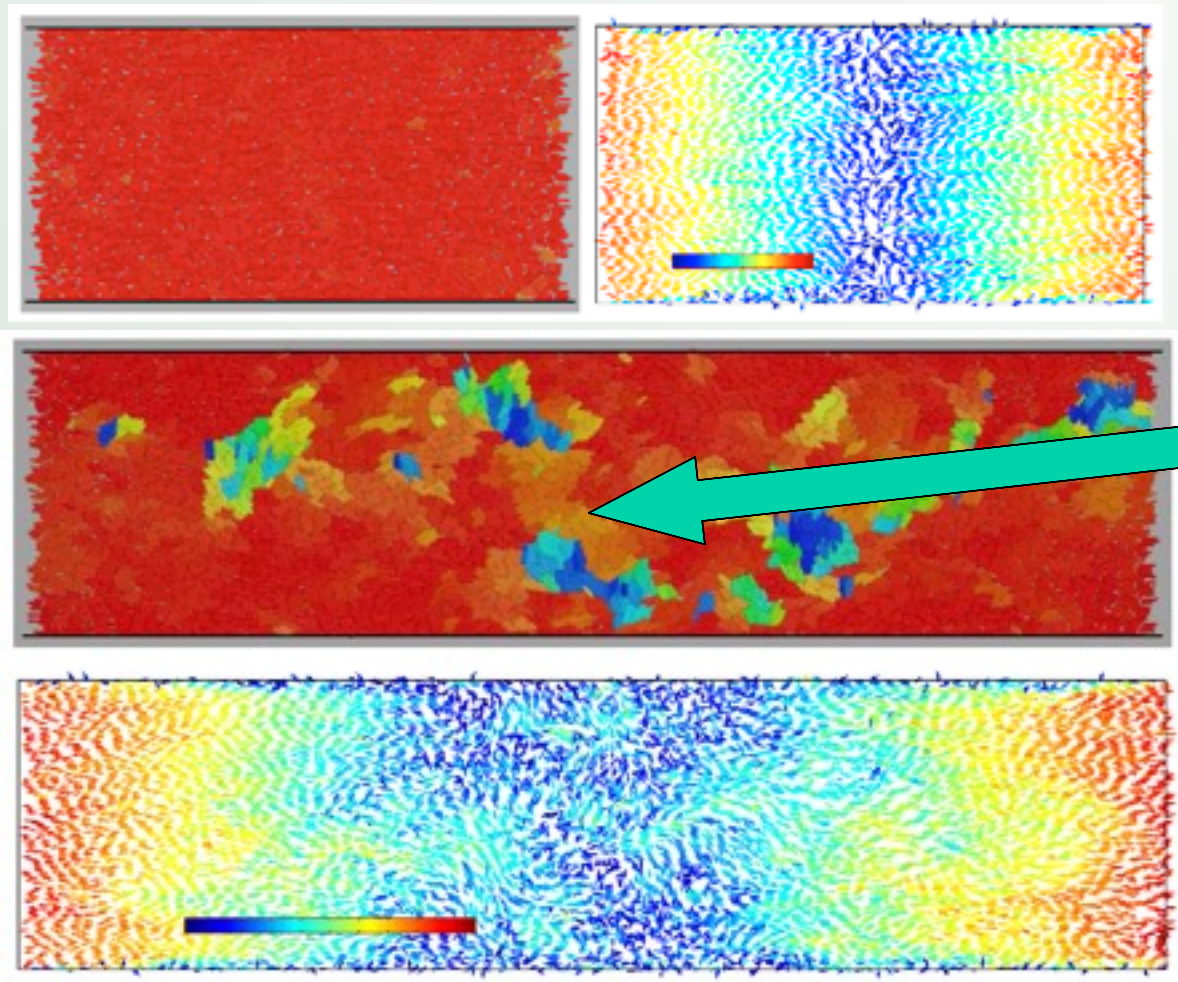
MD simulations

Uniform initial conditions



MD simulations

Different aspect ratios

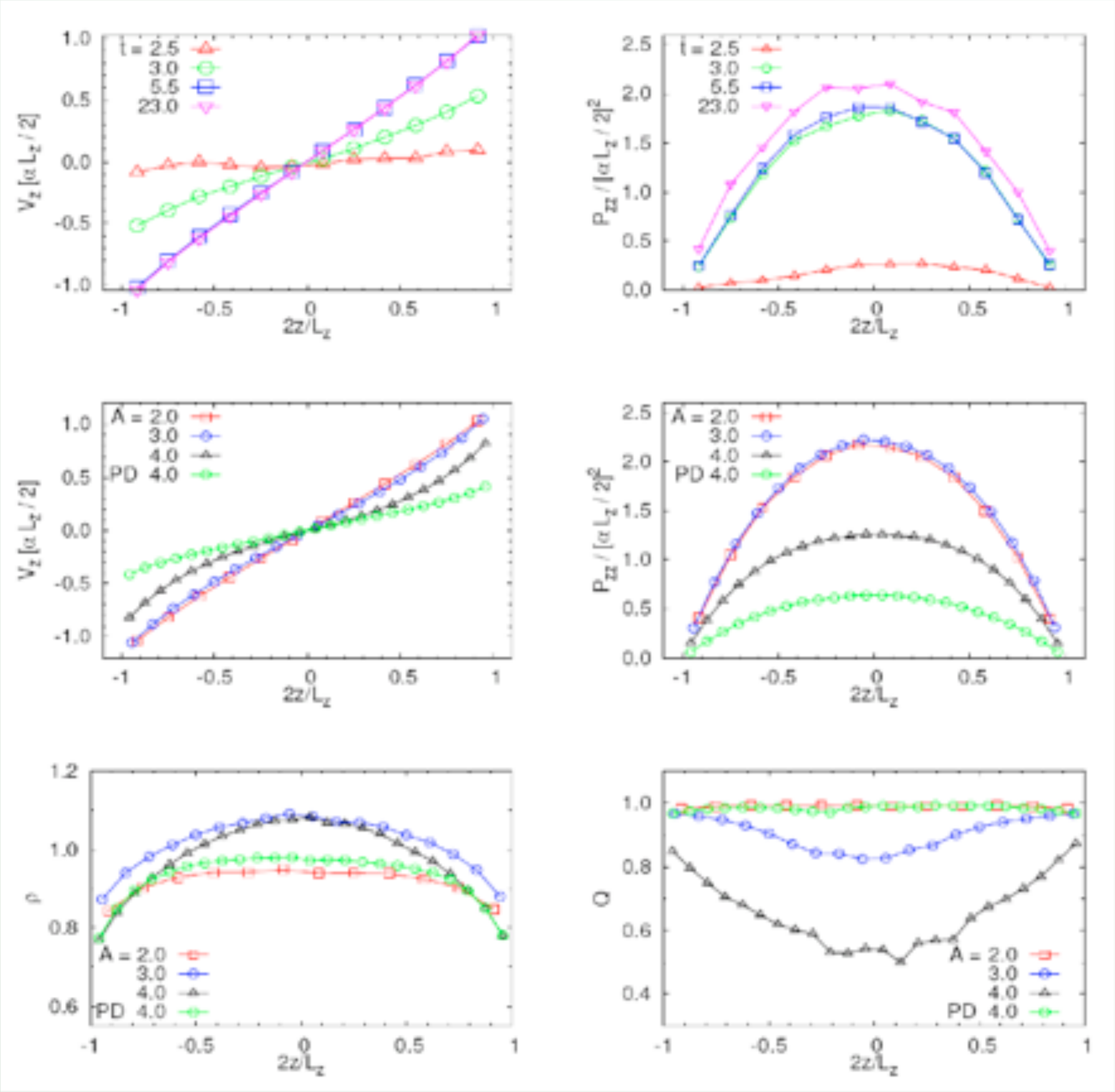


$A = 2$

Persistent disorder

$A = 4$

MD simulations



Uniform initial conditions

Nematodynamics of growing cells

$$\frac{DQ_{\alpha\beta}}{Dt} = (1 - Q^2)[\kappa^{[a]}_{\alpha\gamma} Q_{\gamma\beta} - Q_{\gamma\beta}\kappa^{[a]}_{\alpha\gamma} + B\kappa^{[s]}_{\alpha\beta}]$$

$$\partial_t \rho + \nabla(\rho \mathbf{v}) = \alpha\rho$$

(no thermal motion)

$$\frac{D\rho\mathbf{v}}{Dt} = -\nabla p - \mu\rho\mathbf{v}$$

cf. Doi & Edwards, 1993

$$p = \frac{A\rho}{1 - \rho/\rho_c(Q)}$$

Hard-core repulsion
(critical density is dependent on packing)

$$\rho_c(Q) = R_c + (1 - R_c)Q$$

Nematodynamics equations (1D problem)

$$\partial_t \rho + \partial_z(\rho v) = \alpha\rho$$

$$\partial_t q + v\partial_z q = B(1-q^2)\partial_x v$$

$$\partial_t(\rho v) + v\partial_z(\rho v) = -\partial_z p - \mu\rho v$$

$$q \equiv Q \equiv Q_{xx}, v \equiv v_x$$

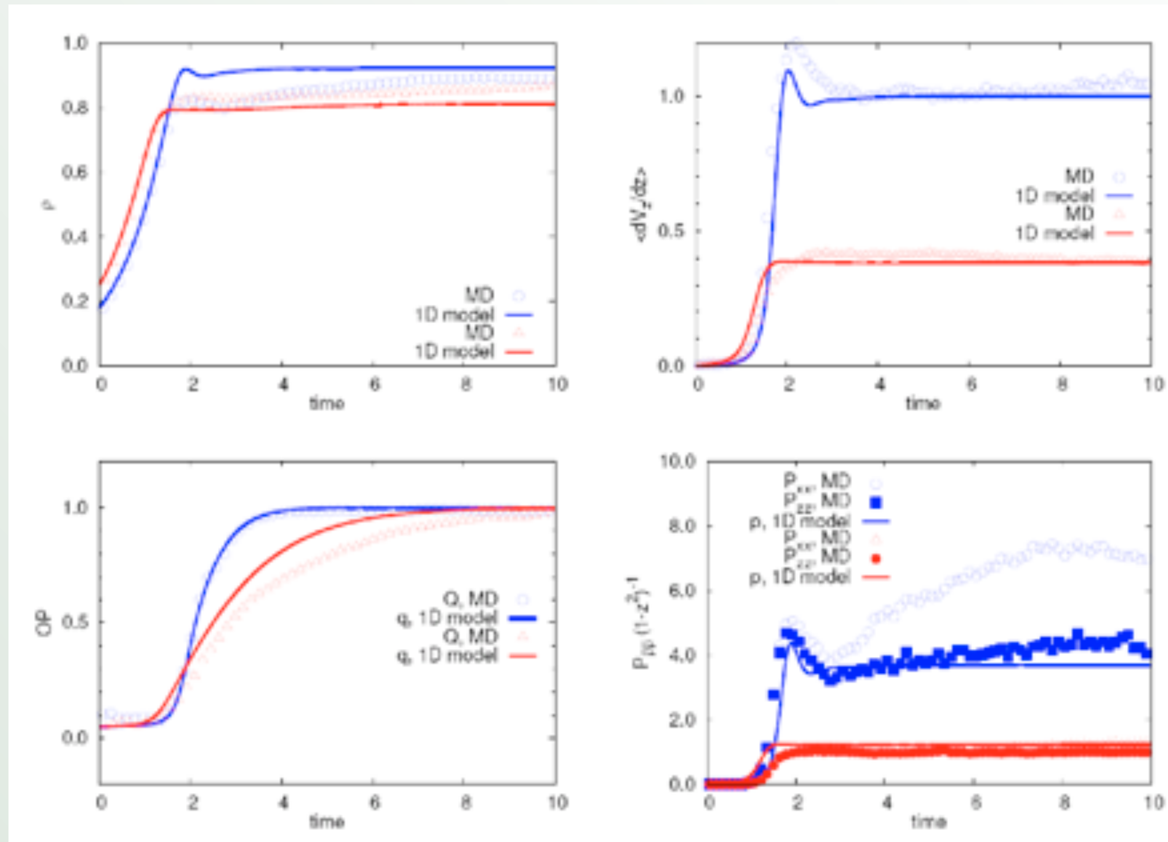
Spatially-uniform dynamics

$$\rho = \rho(t);\ q = q(t);\ v = v_0(t)x;\ p = p_0(t)(1 - x^2 / L^2)$$

$$\dot{\rho} = \rho(\alpha - v_0)$$

$$\dot{q} = B(1 - q^2)v_0$$

$$\dot{v}_0 = 2\rho^{-1}L^{-2}p_0 - (\alpha + \mu)v_0$$



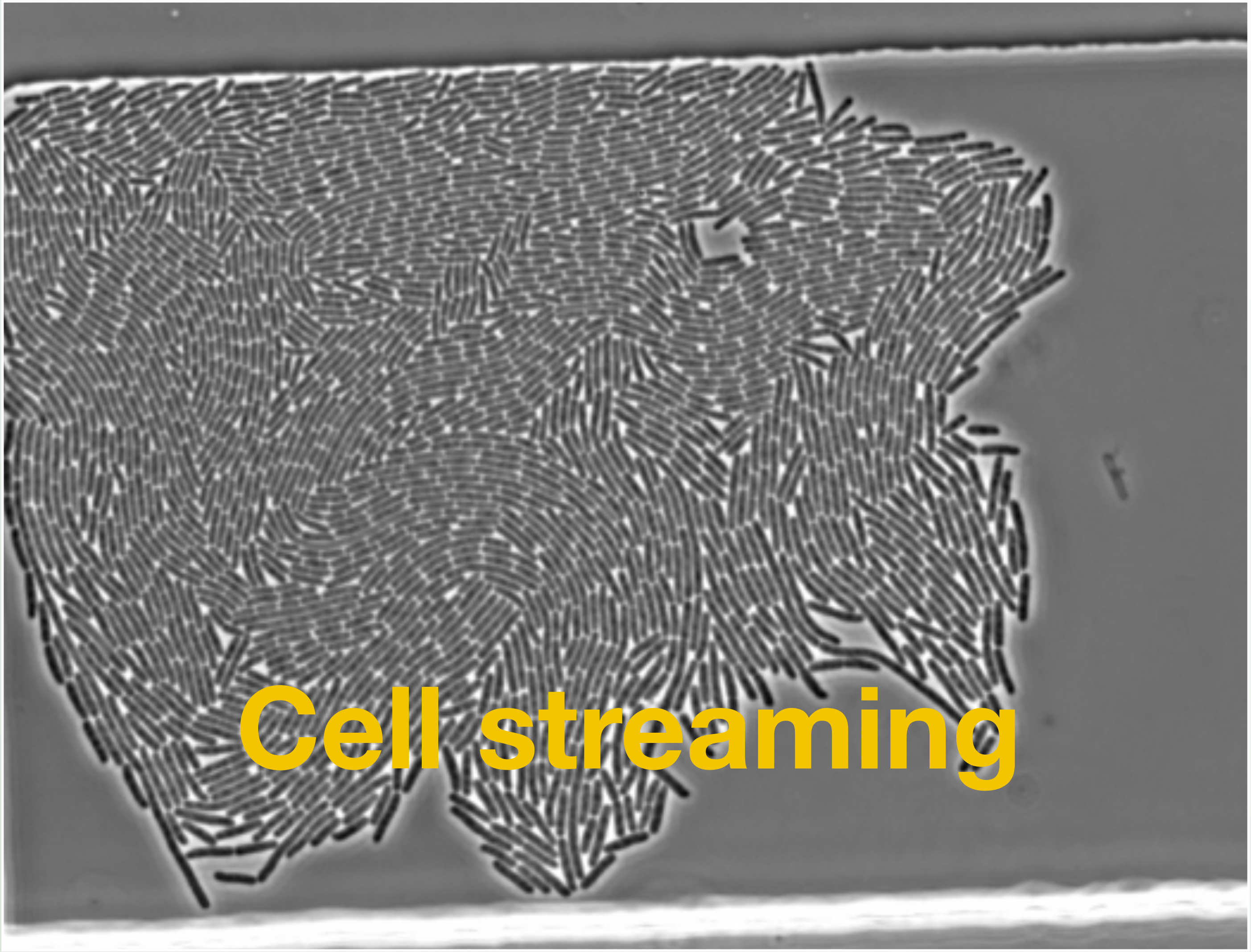
Normalized variables:

$\tilde{t} = \alpha t;\ \tilde{v} = Bv;$

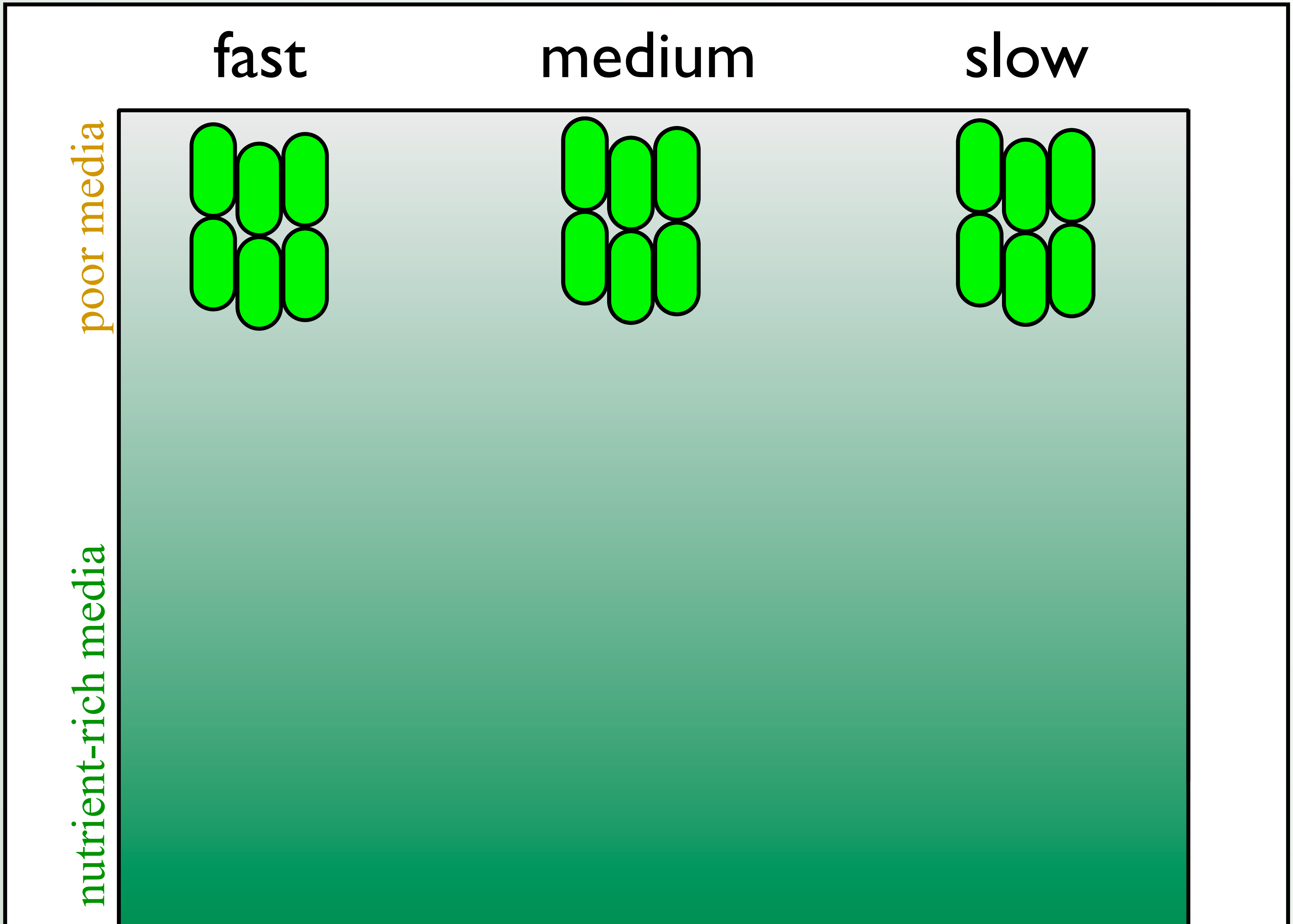
$\tilde{p}_o = p_0 / L^2$

A typical experiment

A typical experiment



Cell streaming mechanism



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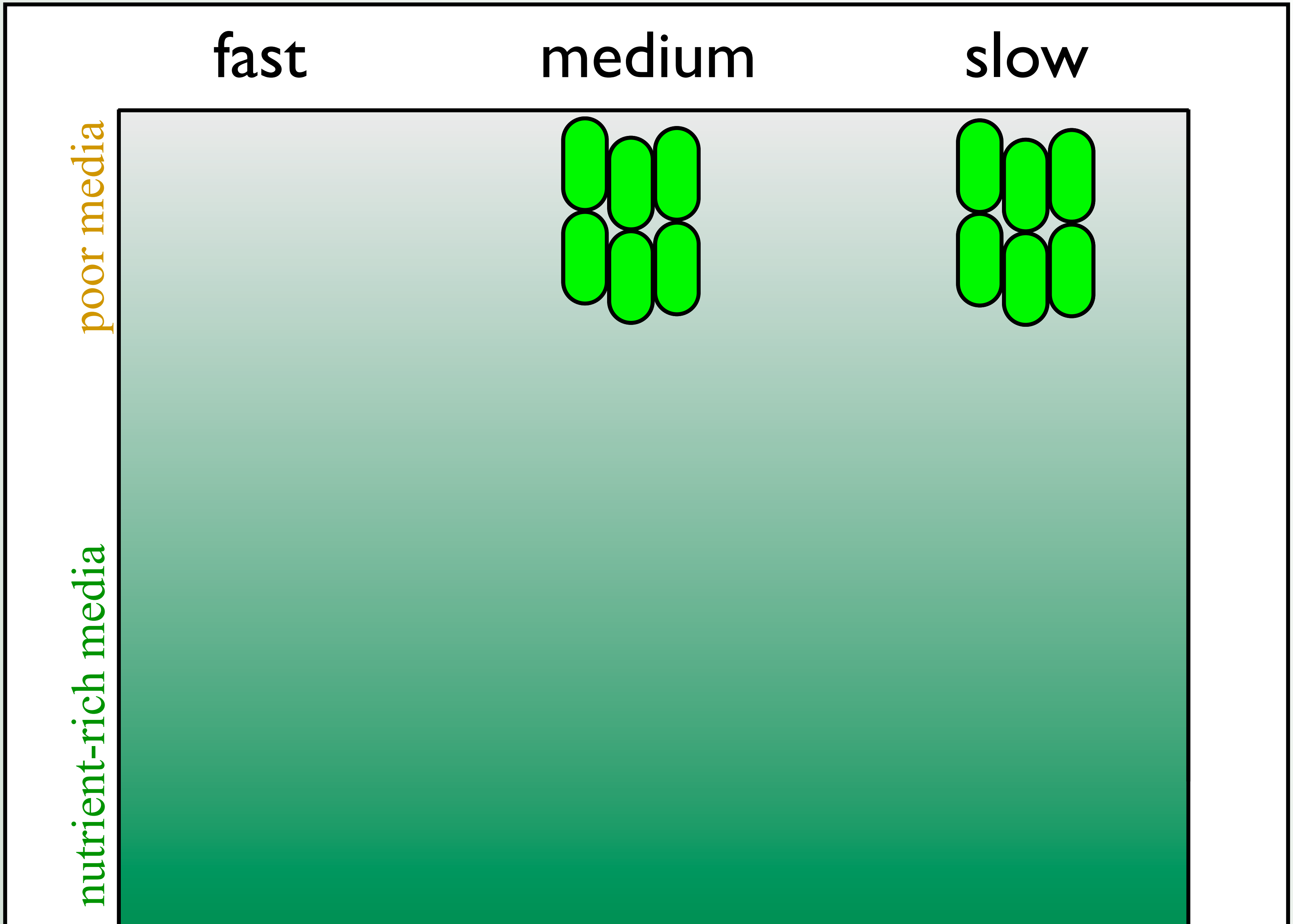

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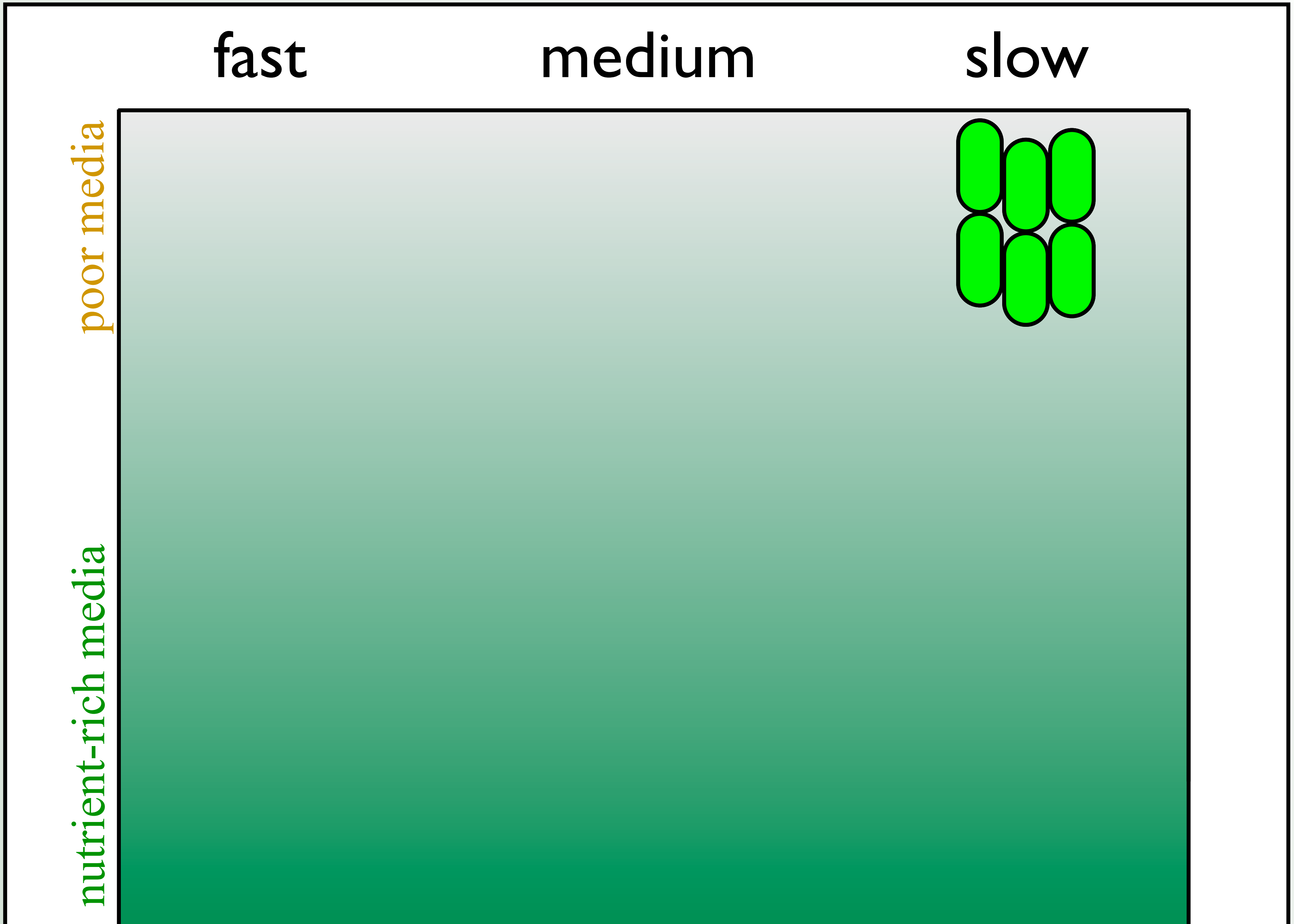

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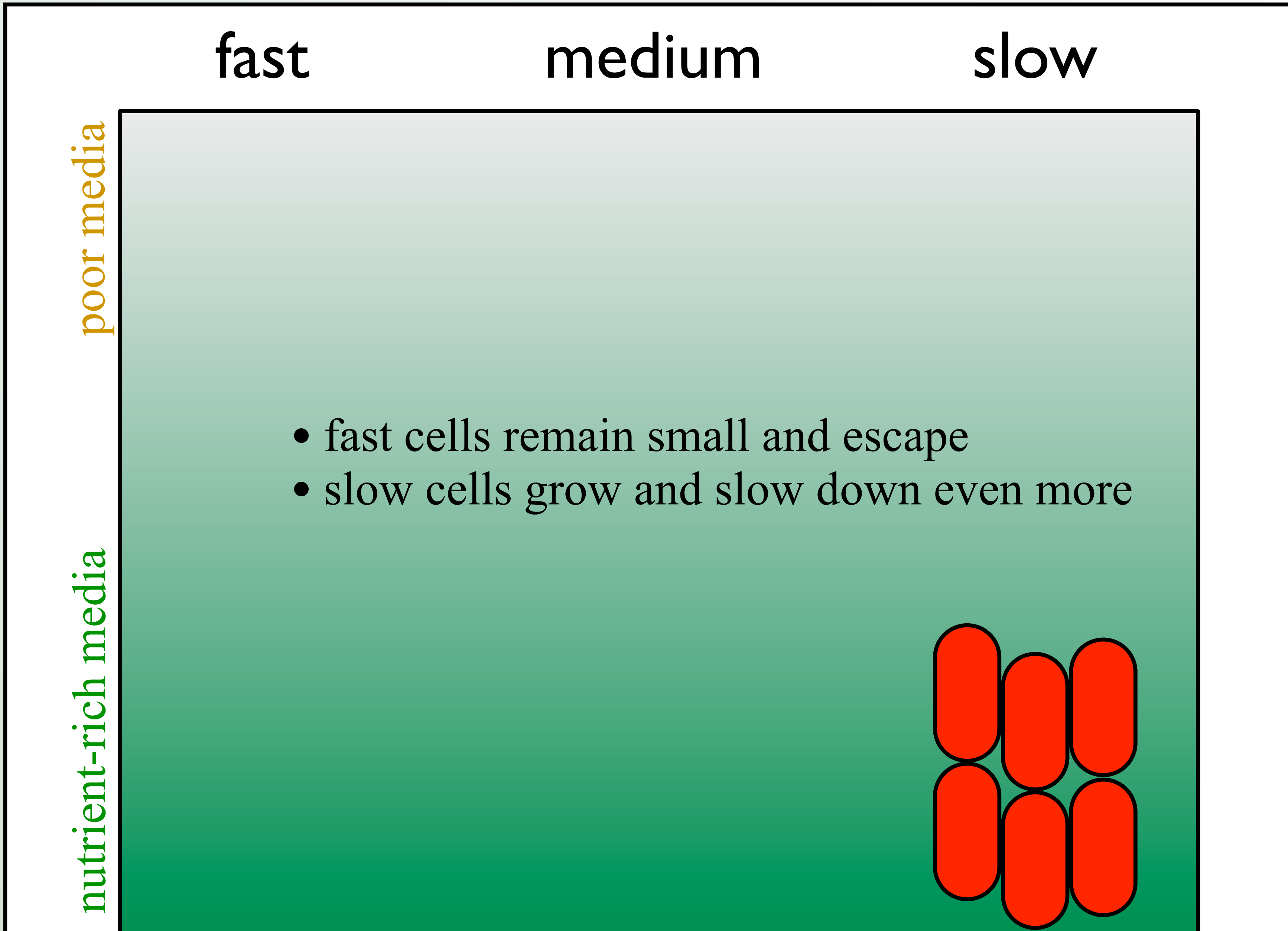

- fast cells remain small and escape
- slow cells grow and slow down even more

MD simulations

size-dependent friction

Newton equations

$$m_i \frac{d\mathbf{v}_i}{dt} = \sum_c \mathbf{F}^{ic} - \boxed{g(f_i)}\mathbf{v}_i$$

$$I_i \frac{d\omega_i}{dt} = R_i \sum_c \mathbf{F}_t^{ic} - \boxed{g(f_i)}\omega_i$$

Cell growth and division

Position-dependent asymptotic cell diameter

$$\frac{df_i}{dt} = \gamma[c(z) - f_i]$$

MD simulations

size-dependent friction

Newton equations

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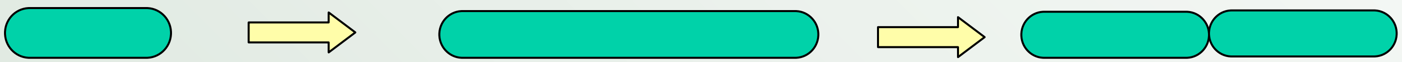

$$l = l_0 \exp[\alpha t], \quad \text{if } \ l > l_m \simeq 2l_0, \ \text{divide}$$

Position-dependent asymptotic cell diameter

$$\frac{df_i}{dt} = \gamma[c(z) - f_i]$$

Continuum modeling

Incompressible fluid dynamics

$$\frac{D\vec{v}}{Dt} = -\vec{\nabla}p - g(f)\vec{v} + \mu\nabla^2\vec{v}$$

$$\frac{Df}{Dt} = \gamma\left(c(\vec{r}) - f\right)$$

$$\vec{\nabla}\cdot\vec{v} = \alpha$$

"Asymptotic" cell size depends on position

Continuum modeling

1D case; overdamped limit

$$\begin{aligned}\frac{\partial p}{\partial z} &= -g(f)v + \mu\frac{\partial^2 v}{\partial z^2}\\ \frac{\partial f}{\partial t} + v\frac{\partial f}{\partial z} &= \gamma\left(c(z) - f\right)\\ \frac{\partial v}{\partial z} &= \alpha\end{aligned}$$

linear velocity profile:

$$v(z,t) = \alpha z + v_0(t)$$

Continuum modeling

1D case; overdamped limit

$$
\begin{aligned}
\frac{\partial p}{\partial z} &= -g(f)v + \mu \frac{\partial^2 v}{\partial z^2} \\
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\end{aligned}
$$

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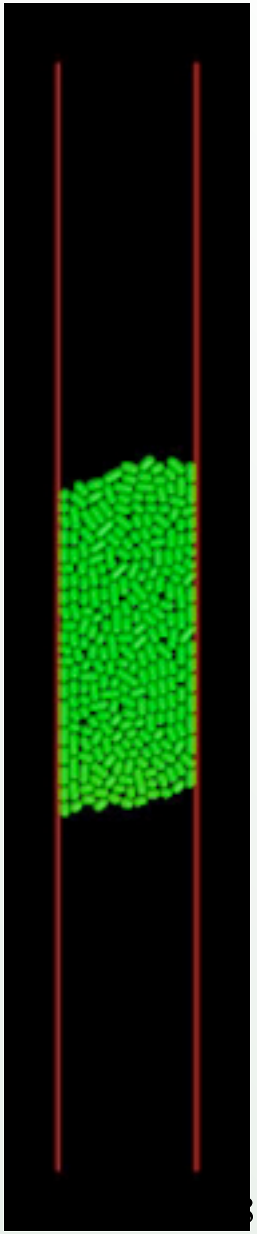
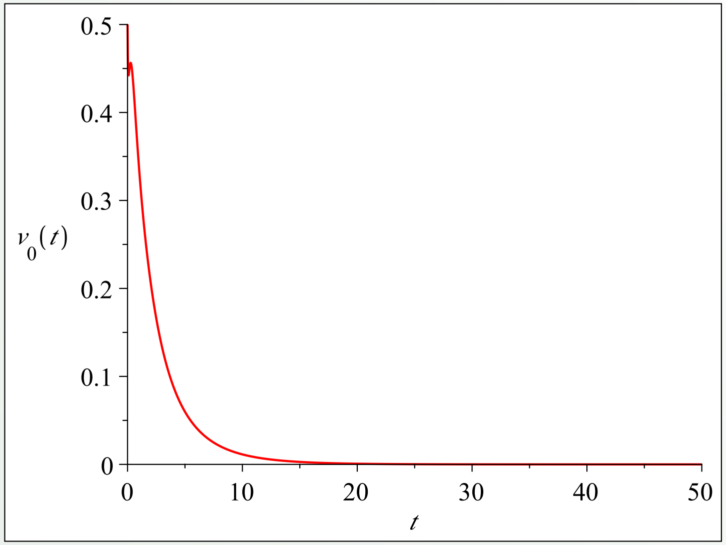


Narrow channel: symmetric regime



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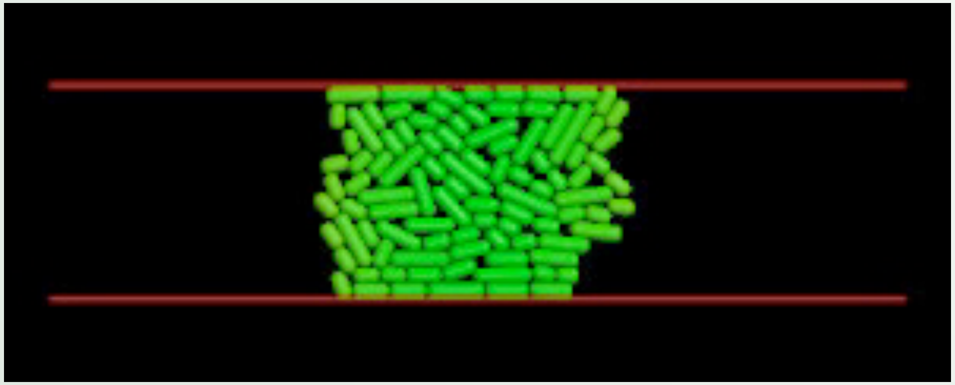

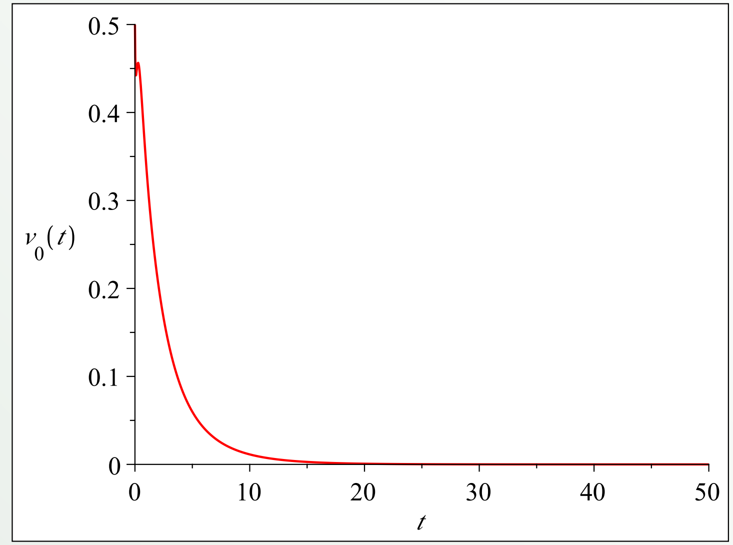

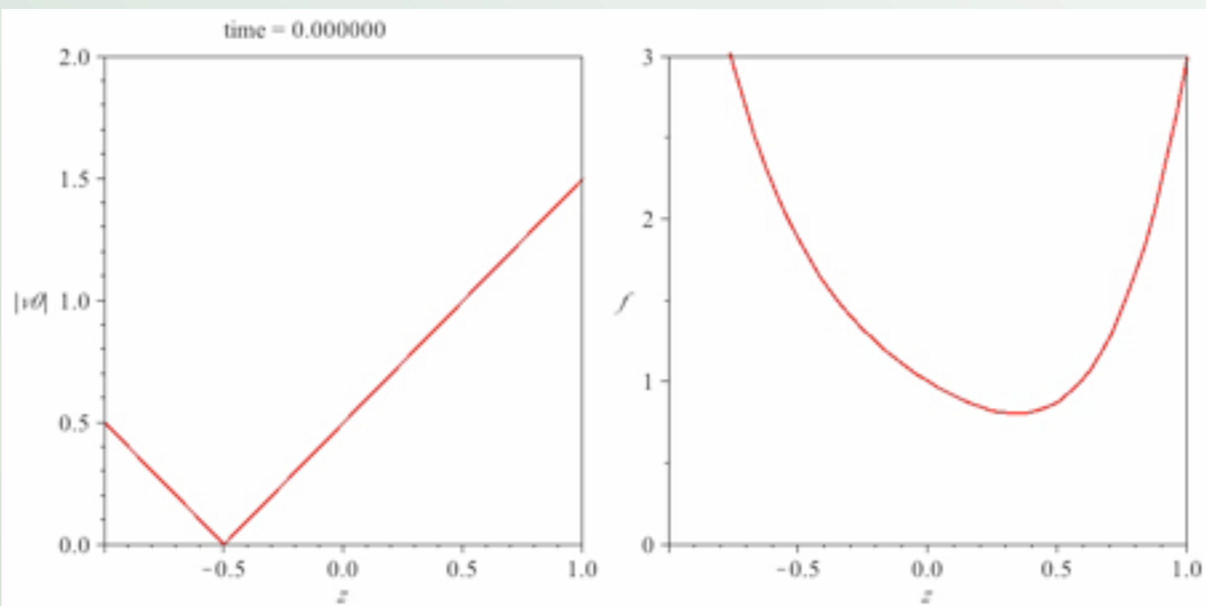

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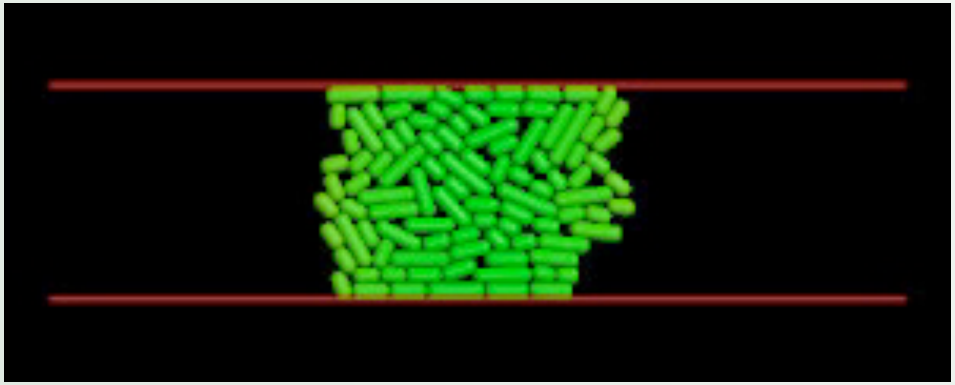
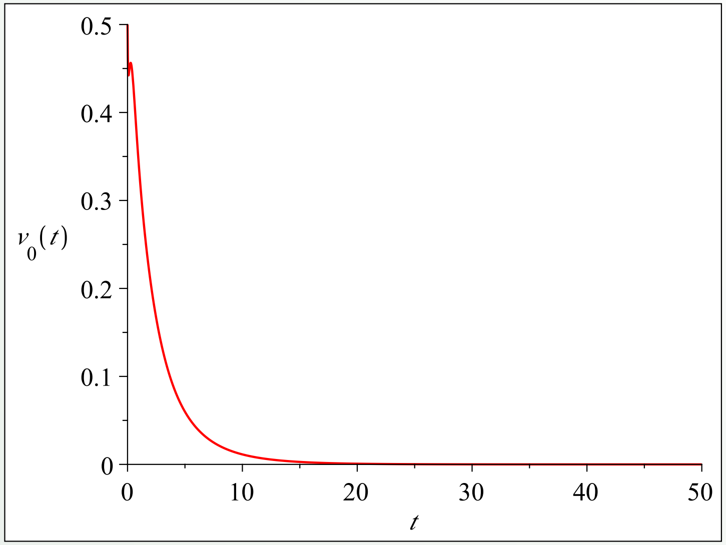
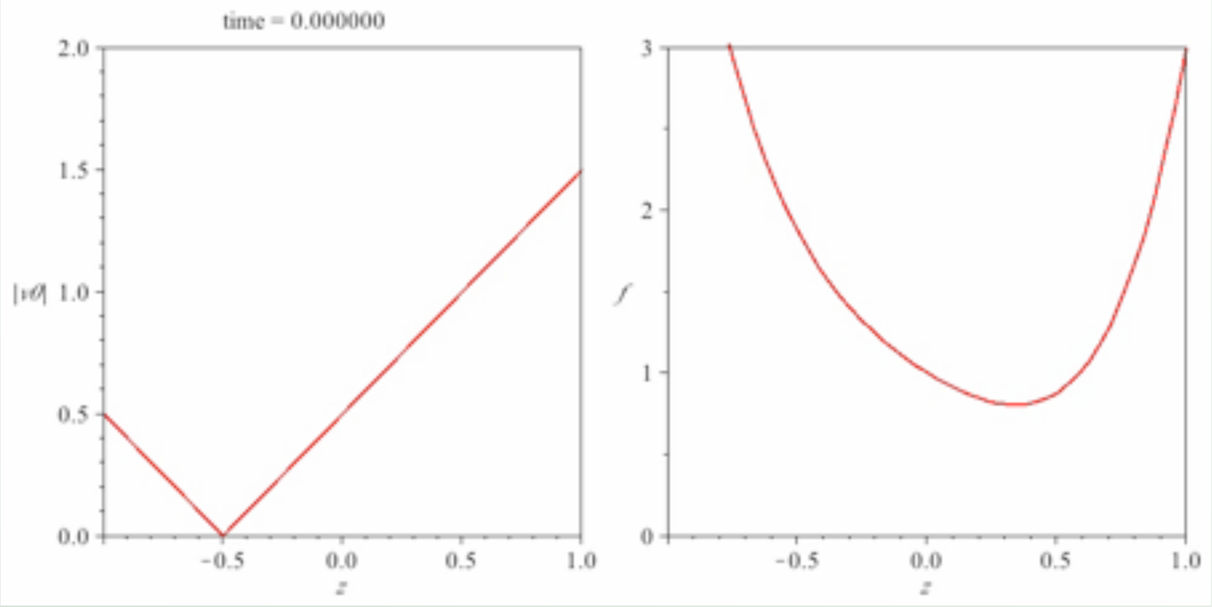
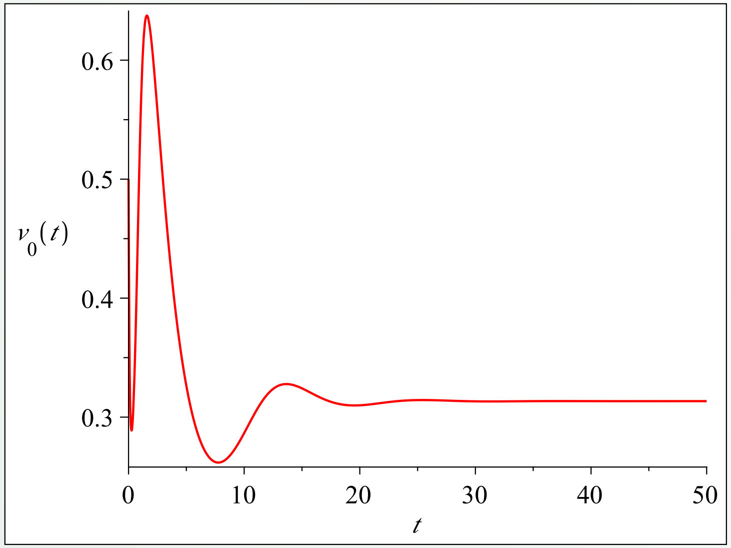


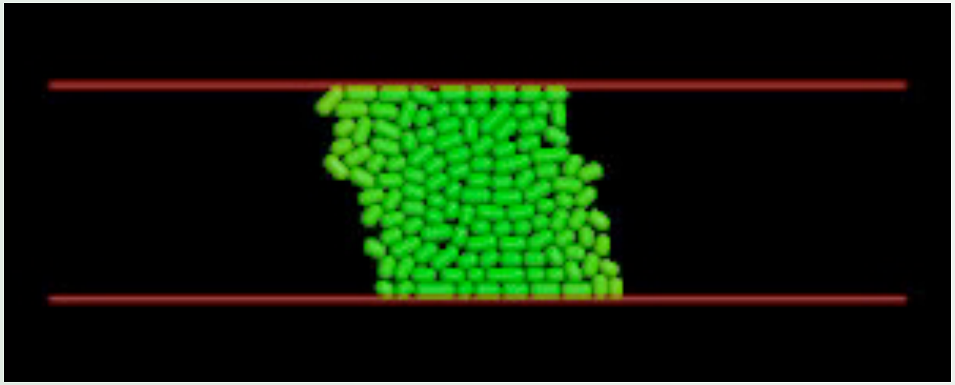


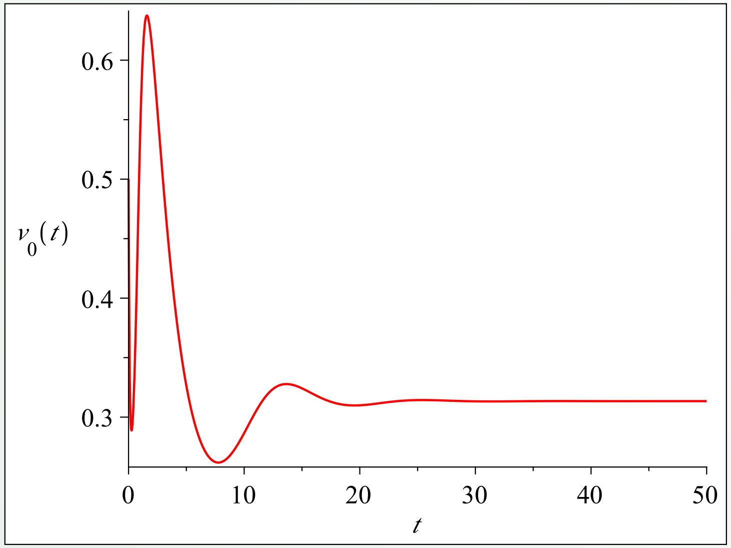


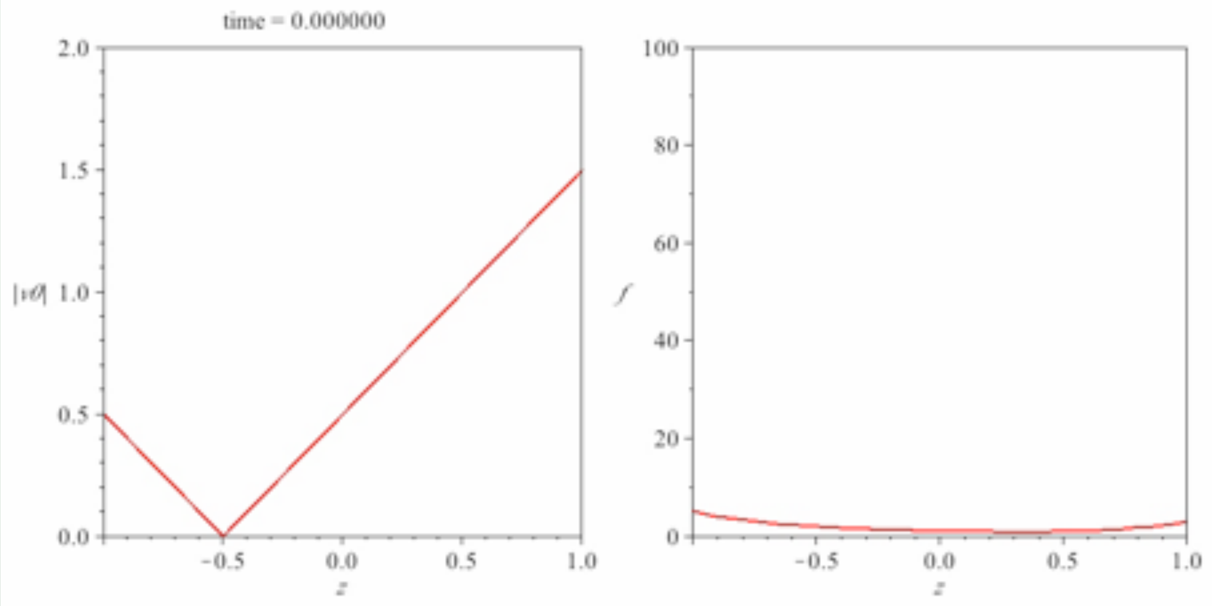
Narrow channel: asymmetric regime



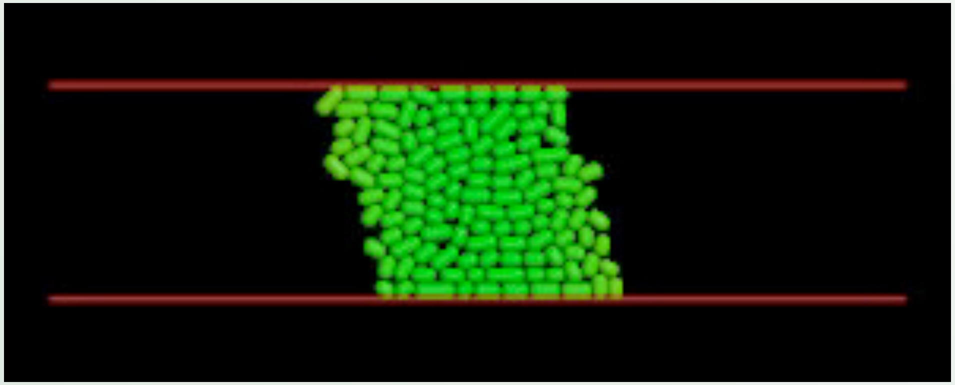
Narrow channel: asymmetric regime

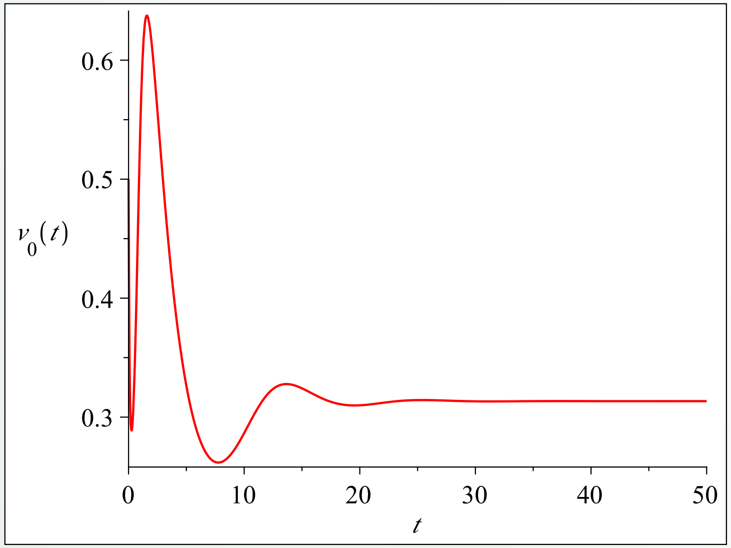


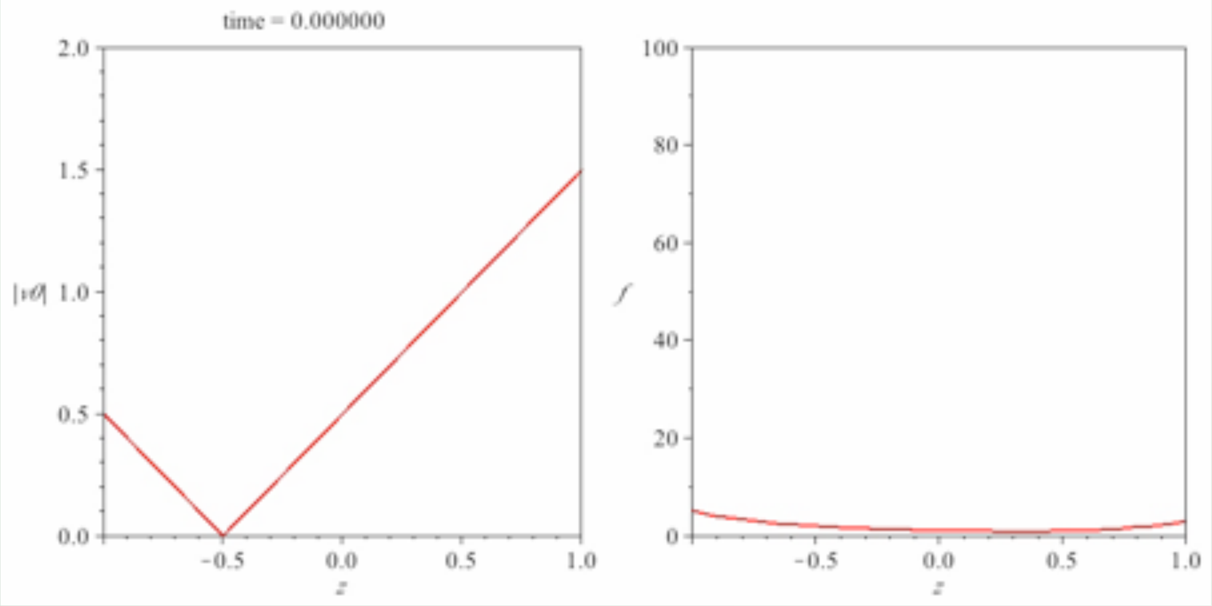




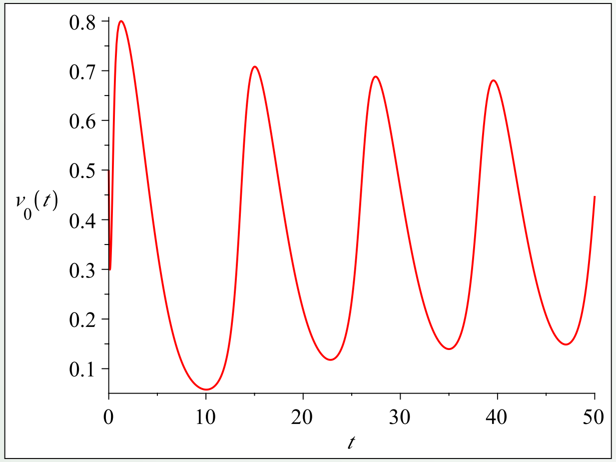
Narrow channel: asymmetric regime



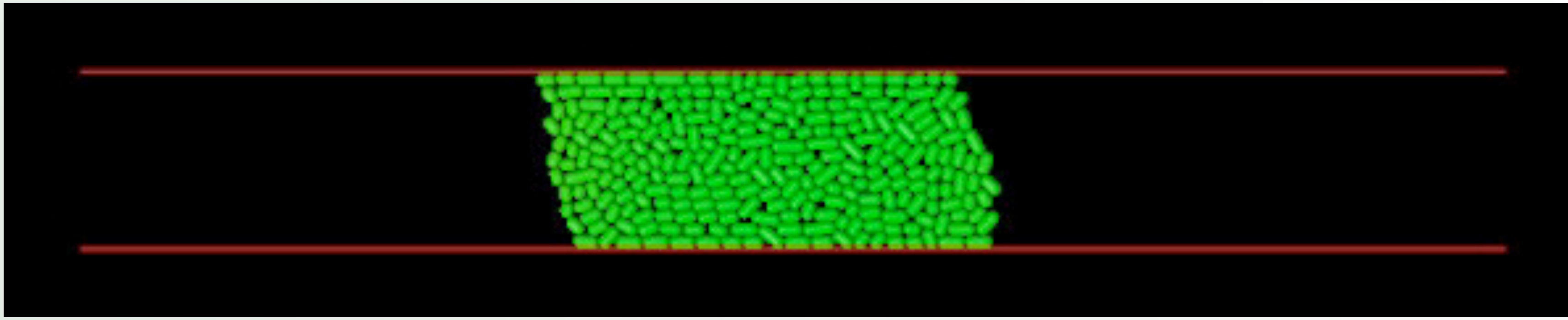


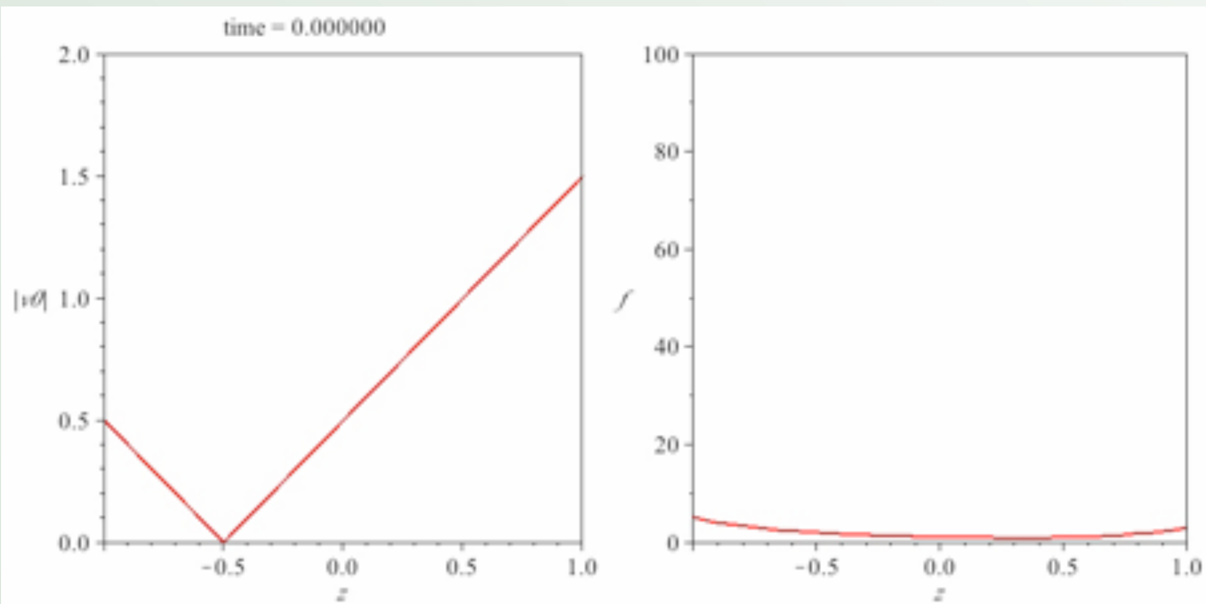


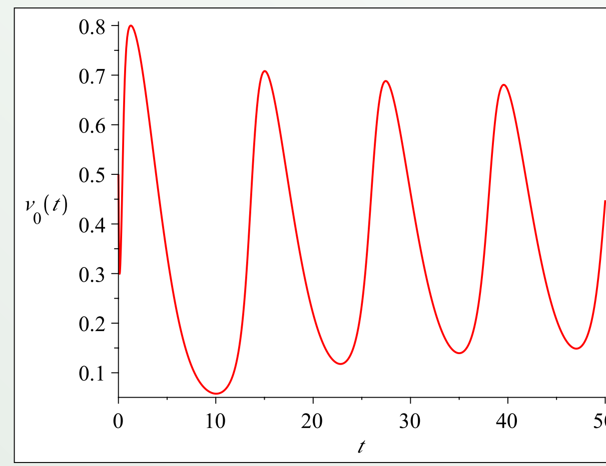
Narrow channel: oscillatory regime



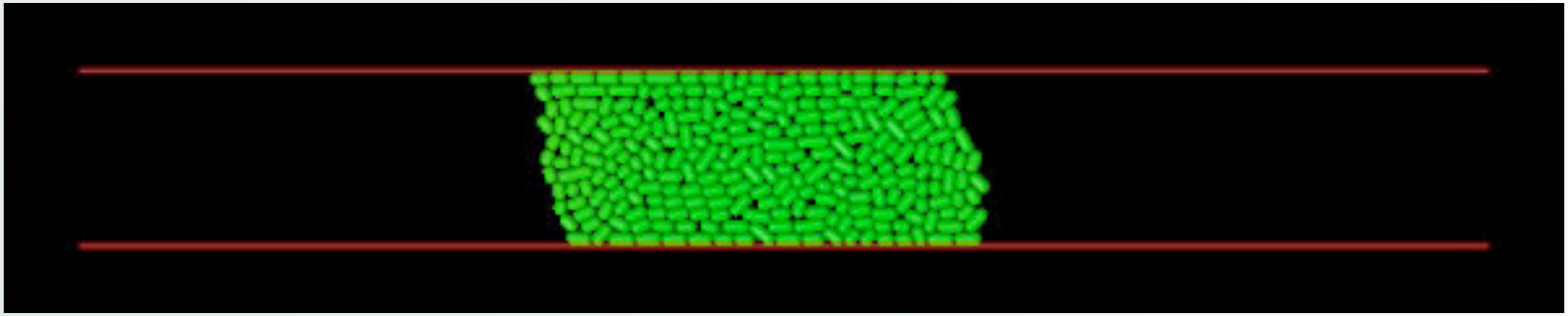
Narrow channel: oscillatory regime

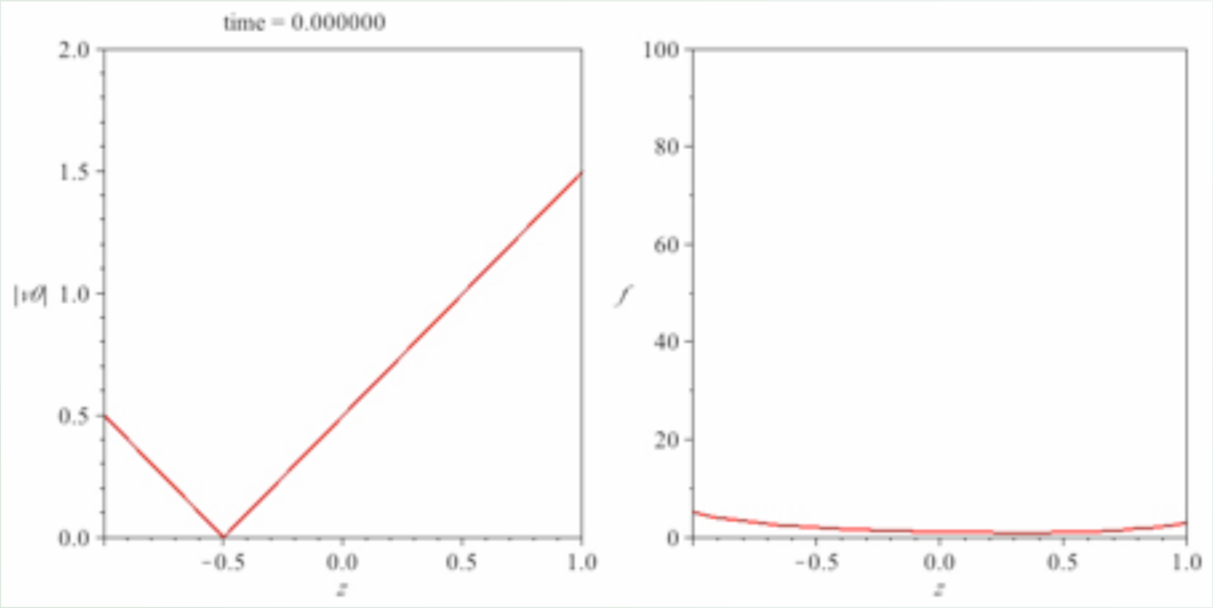


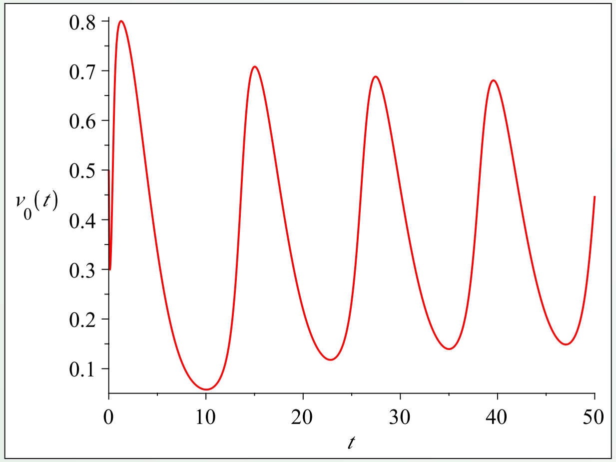




Narrow channel: oscillatory regime



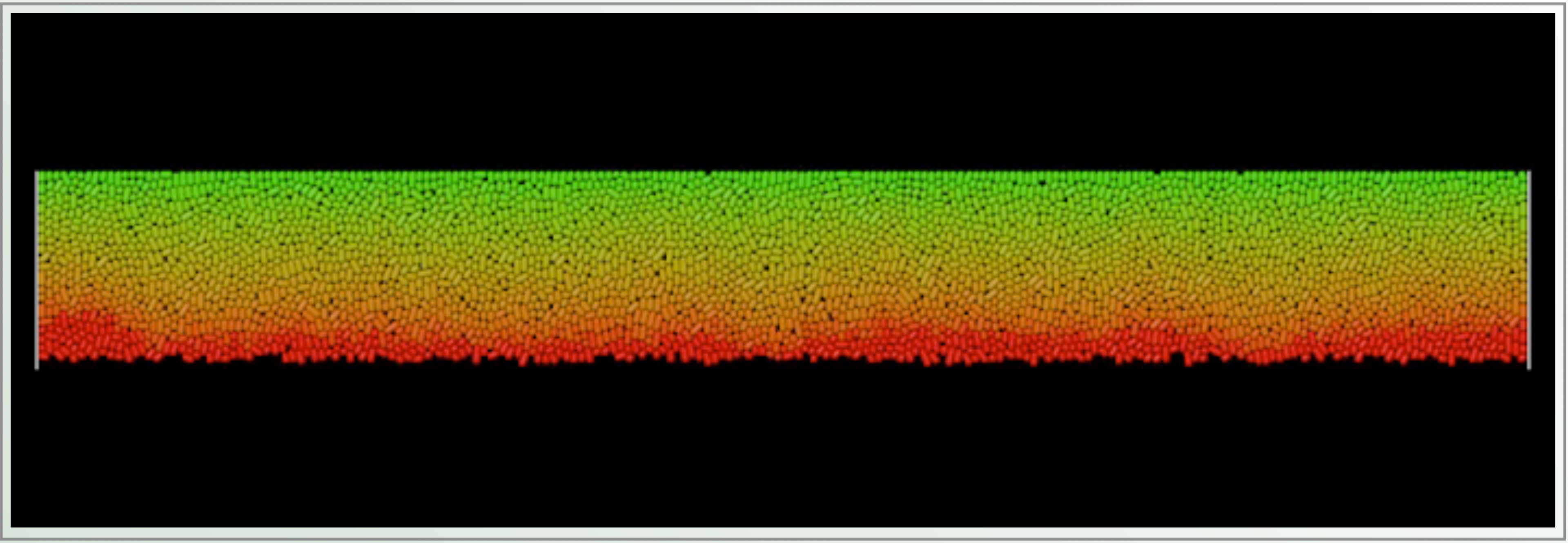




Long "side trap"

Short rods, A=2

Long “side trap”

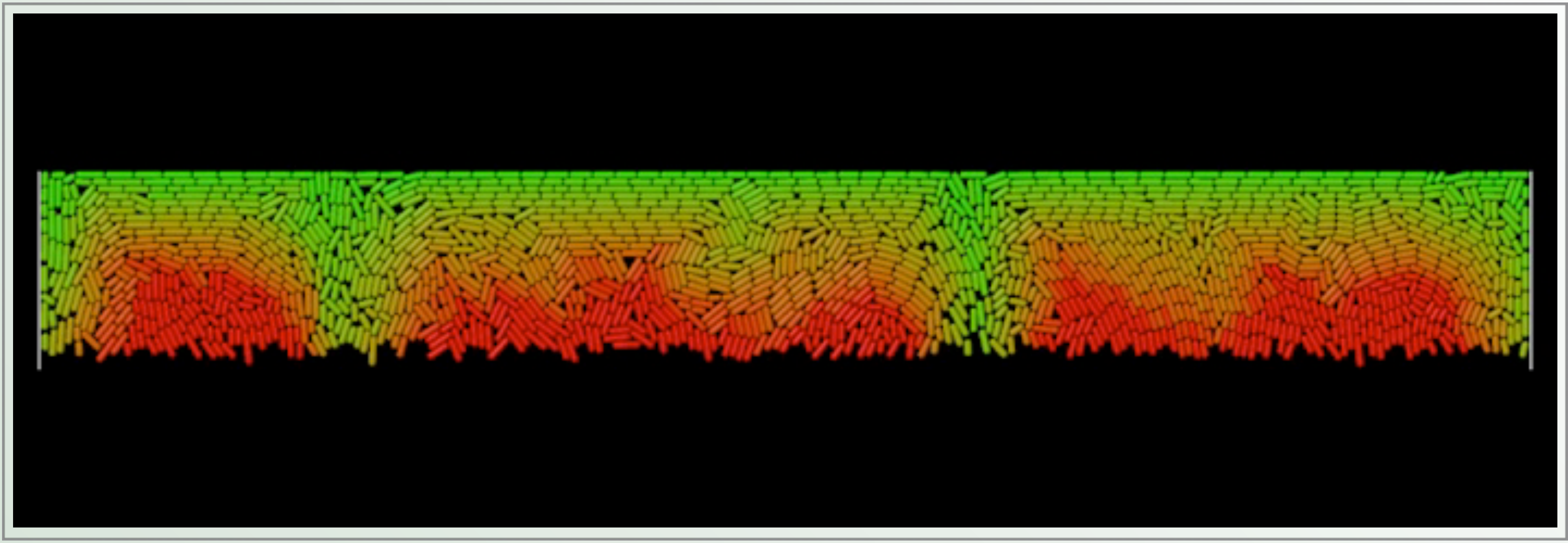


Short rods, A=2

Long “side trap”

Long rods, A=5

Long “side trap”

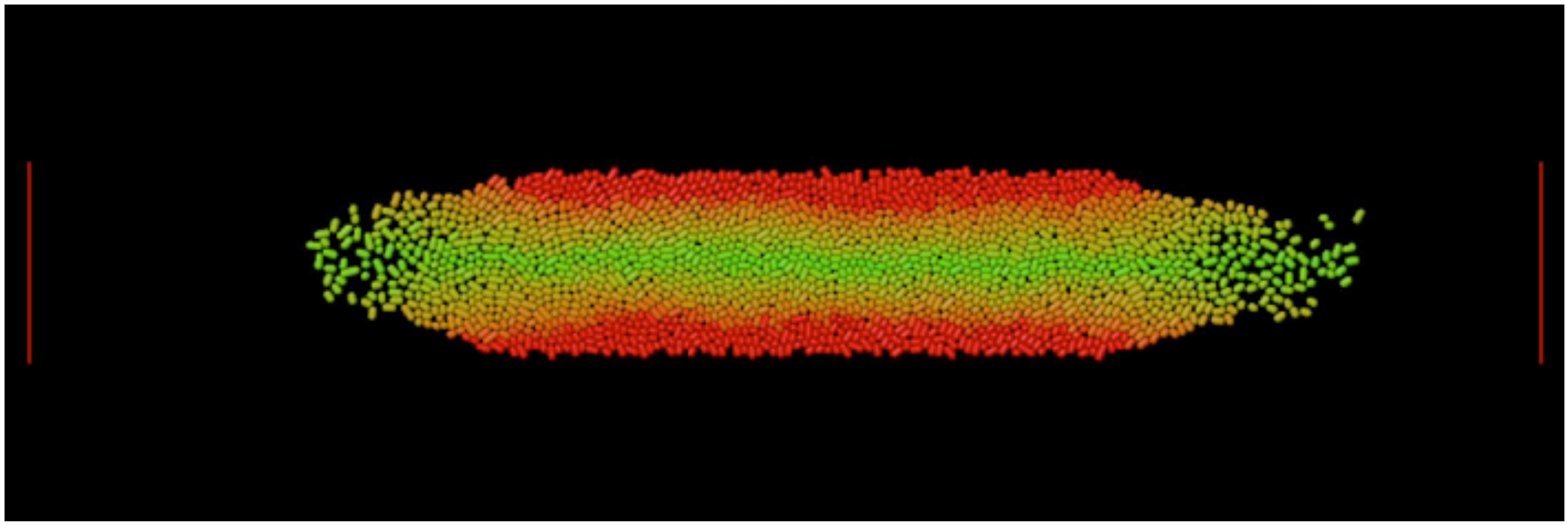


Long rods, A=5

Long “open trap”

Short rods, A=2

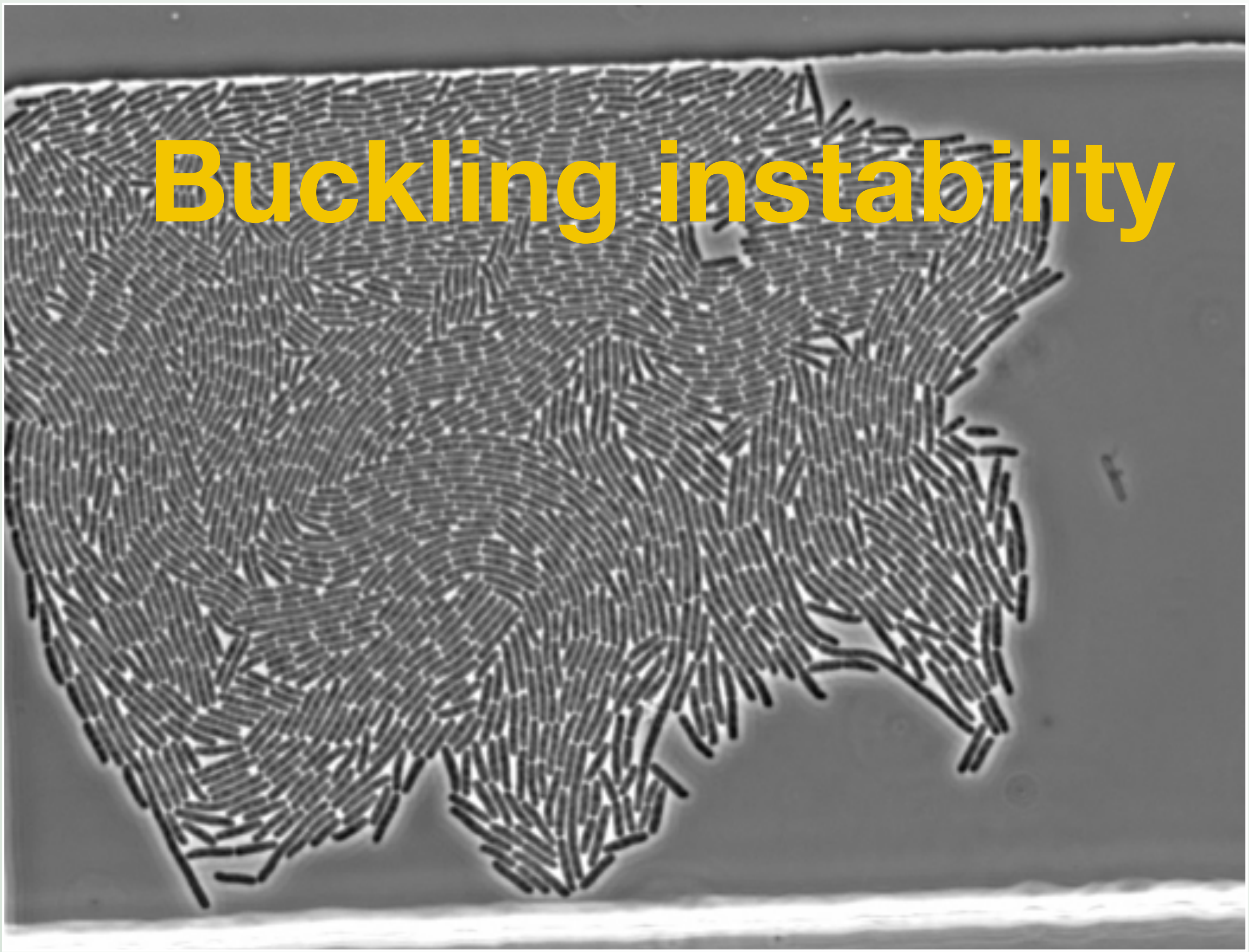
Long "open trap"



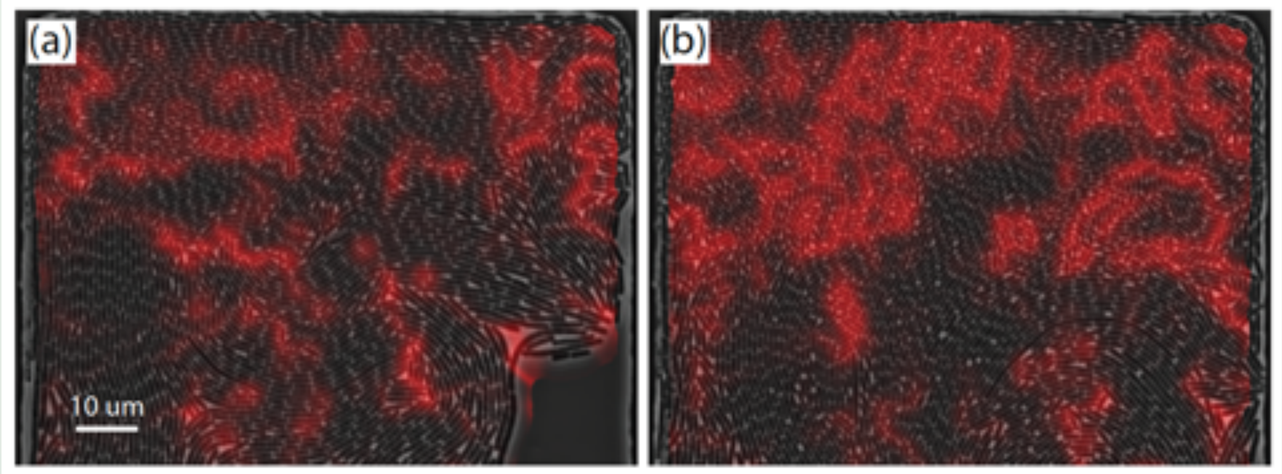
Short rods, A=2

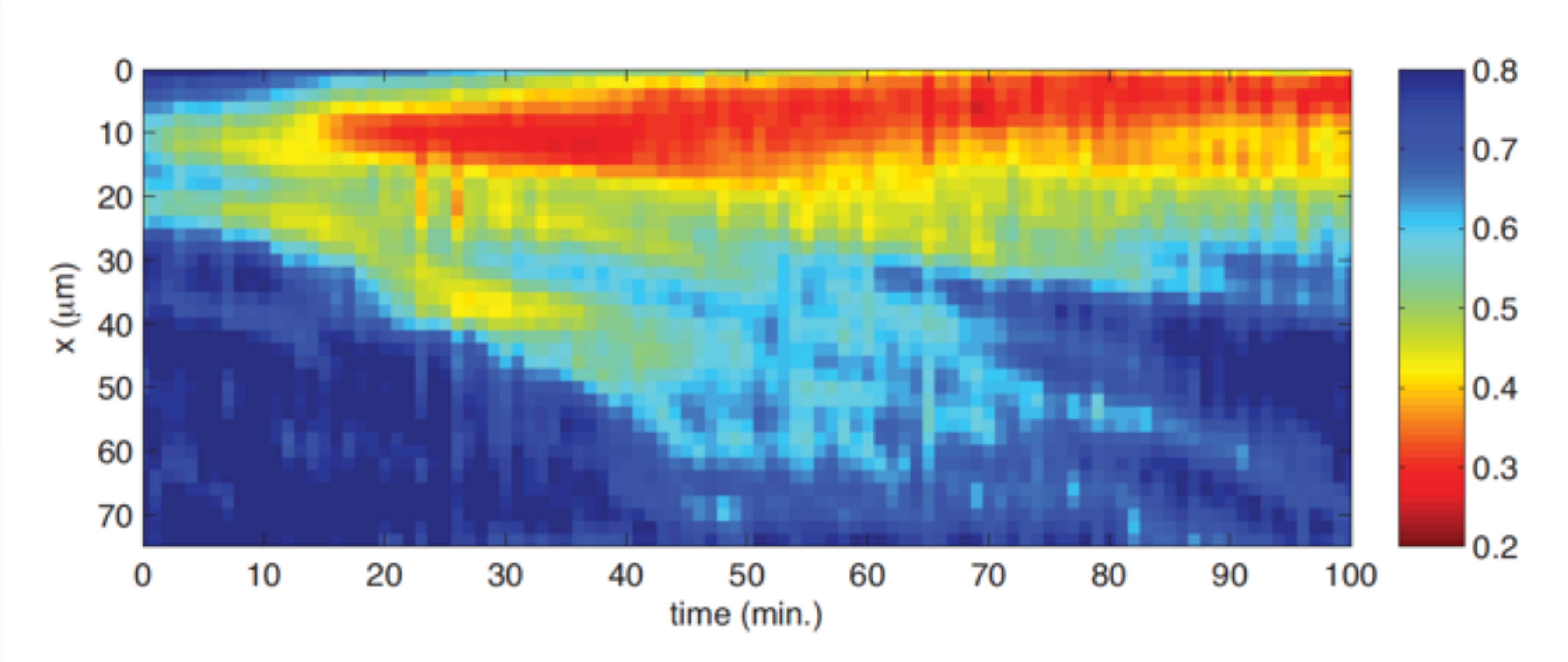
A typical experiment

A typical experiment

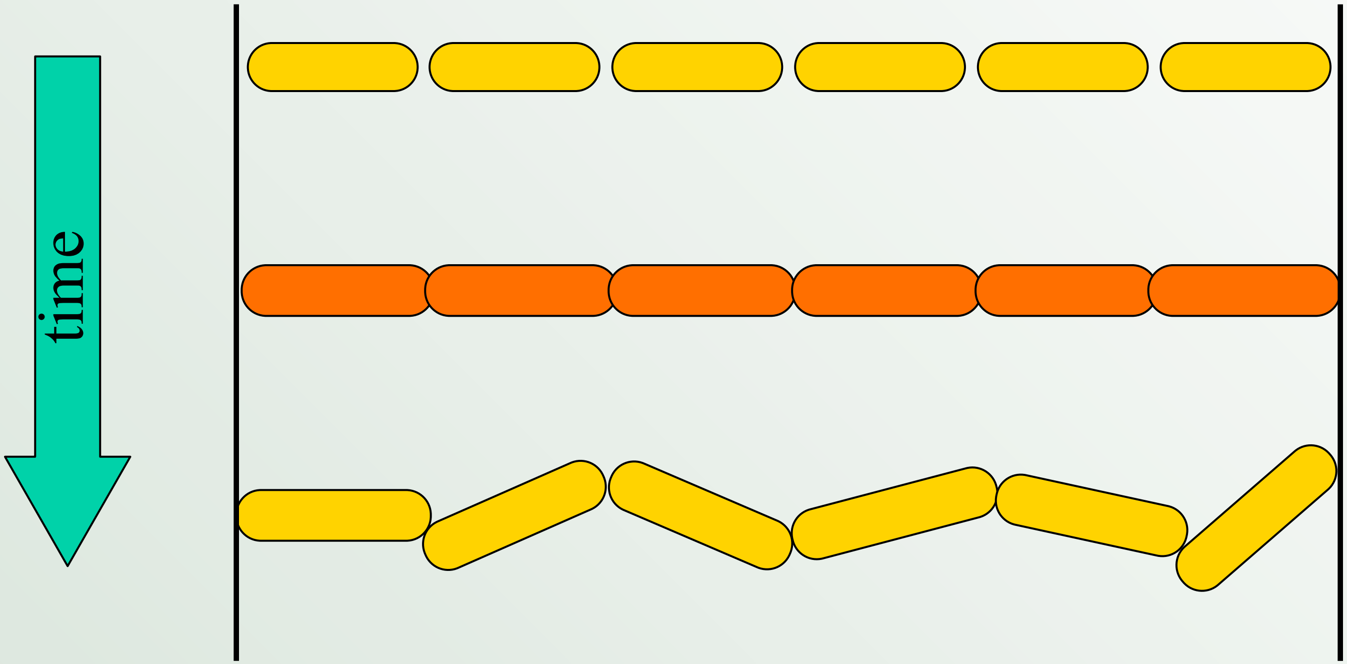


Orientational order parameter





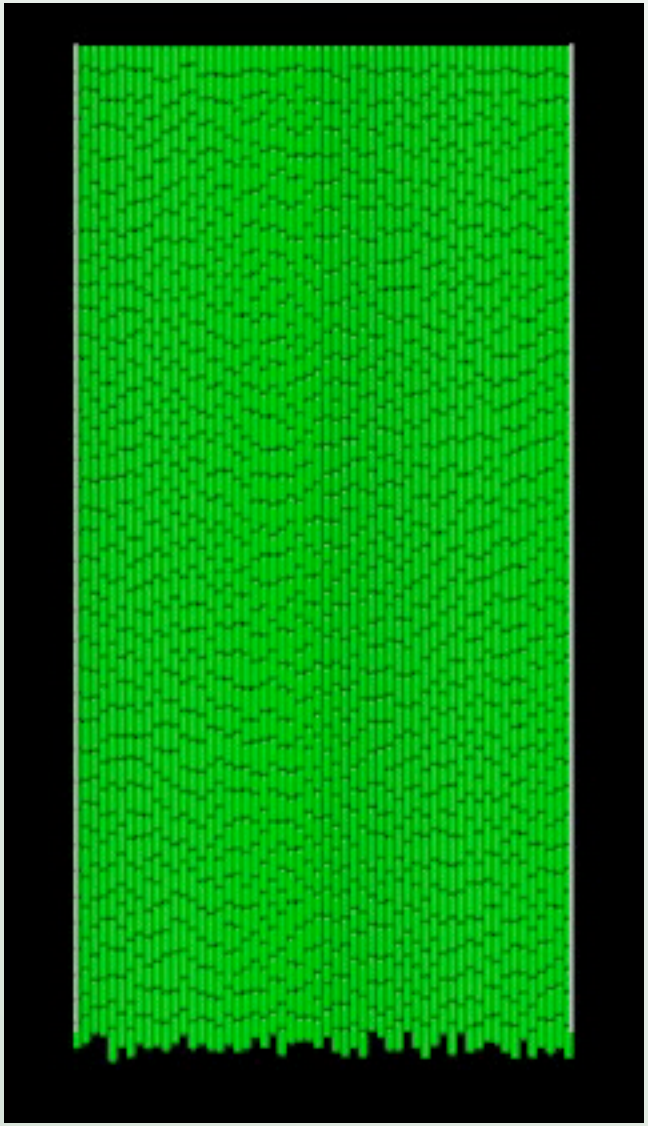
Cell buckling mechanism

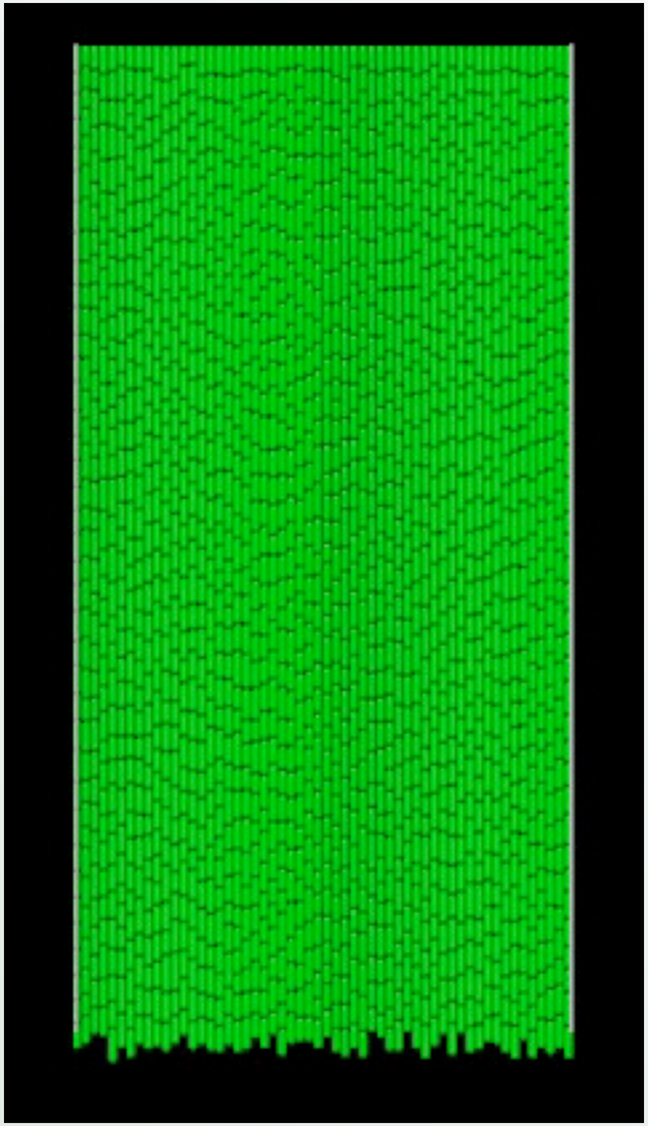


- cell growth increases longitudinal component of stress tensor
- lateral displacement relieves compression

MD simulations

A=4



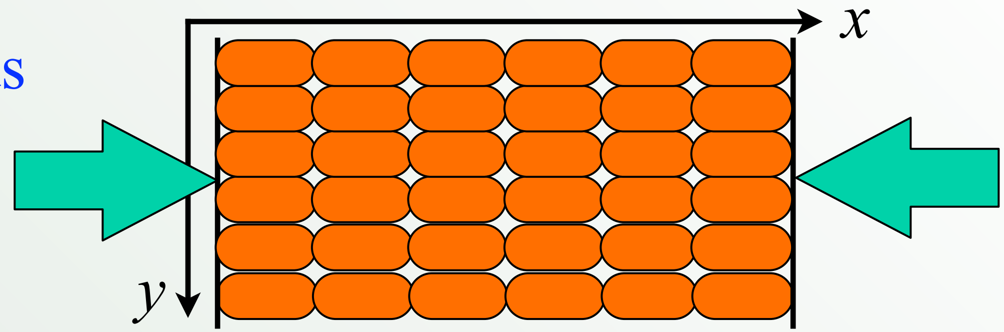


A=3

A=6

Continuum modeling

Compressed non-growing rods



Elastic energy

$$F_{el} = \frac{1}{2}\int d\mathbf{r}\left[\lambda_{xx}u_{xx}^2 + \lambda_{yy}u_{yy}^2 + \lambda_{xy}u_{xy}^2 + \lambda_1 u_{xx}u_{yy} + \xi(\partial_x^2 u_y)^2\right]$$

Strain tensor

$$u_{ij} = \frac{1}{2}\left(\partial_j u_i + \partial_i u_j + \partial_i u_k \partial_j u_k\right)$$

$$u_{xx} = -p_x/\lambda_{xx} + \frac{1}{2}(\partial_x \tilde{u}_y)^2, \quad u_{xy} = \frac{1}{2}\partial_x \tilde{u}_y$$

$$w = \tilde{u}_y$$

$$F_{el} = \frac{1}{2}\int d\mathbf{r}\left[p_x^2/\lambda_{xx} - p_x(\partial_x w)^2 + \frac{1}{4}\lambda_{xy}(\partial_x w)^2 + \xi(\partial_x^2 w)^2\right]$$

lateral displacement relieves compression

Continuum modeling
(dynamical model)

$$L = \frac{1}{2}\int d\mathbf{r}\, \dot{w}^2 - F_{el}$$ Lagrangian

$$F_d = \mu \int d\mathbf{r} (\dot{w})^2/2$$ Dissipative function (due to friction)

$$\frac{\partial}{\partial t}\left(\frac{\delta L}{\delta \dot{w}}\right) - \frac{\delta L}{\delta w} = -\frac{\delta F_d}{\delta \dot{w}}$$ Euler-Lagrange equation

$$\boxed{\mu \partial_t w = (\lambda_{xy}/4 - p_x)\partial_x^2 w - \xi \partial_x^4 w}$$

$$s = \mu^{-1}[(p_x - \lambda_{xy}/4)k^2 - \xi k^4]$$ growth rate

Continuum modeling - growing rods

Linear velocity profile

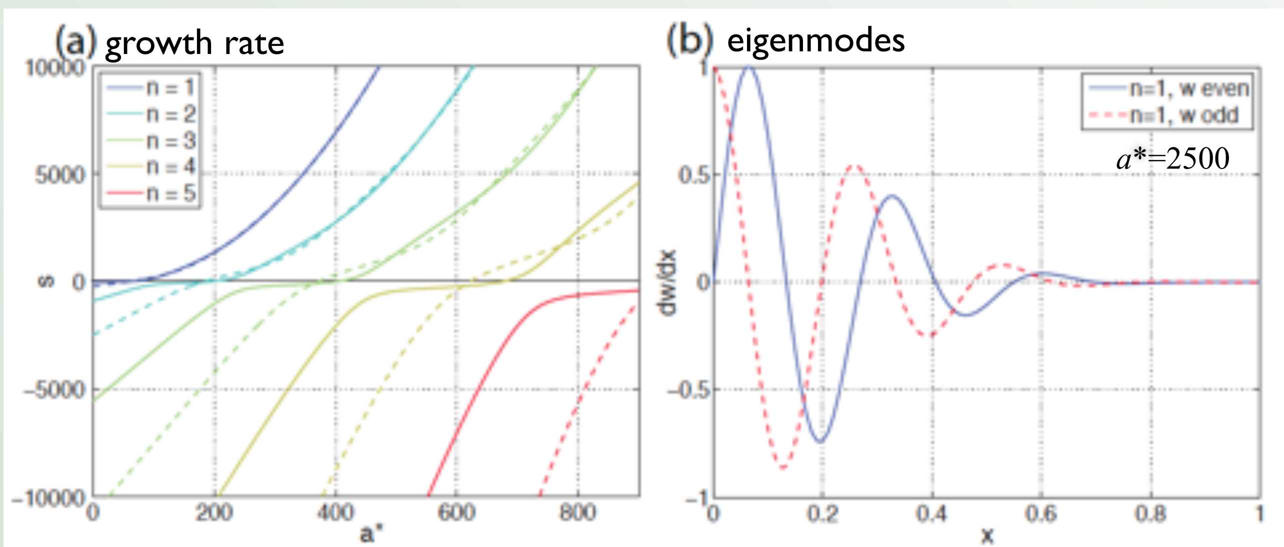
$$v_x = ax$$

Parabolic pressure profile

$$p_x = \frac{1}{2}\mu a(x^2 - L_x^2/4)$$

Dynamic equation

$$\partial_t w + ax\partial_x w = -[\frac{a}{2}(L_x^2/4 - x^2) - \lambda_{xy}/4\mu]\partial_x^2 w - \frac{\xi}{\mu}\partial_x^4 w$$



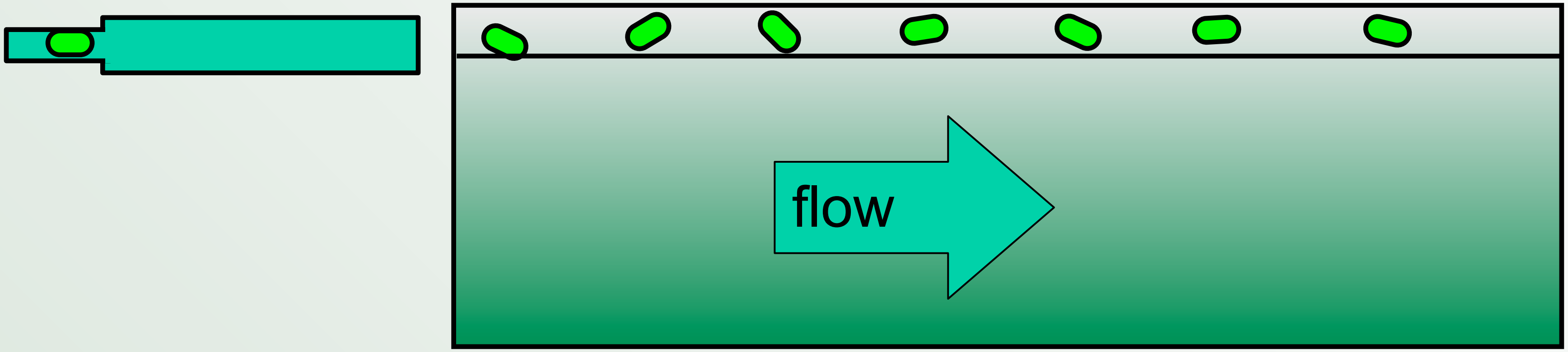
Conclusions

- Cell growth and ensuing expansion flow generates ordering in populations
- Size- and position-dependent friction leads to *streaming* instability
- Anisotropic stresses generated by cell growth lead to *buckling*.
- Experiments in microfluidic chambers, MD simulations, and continuum theory based on nematodynamics and elasticity theory are in qualitative agreement.
- Growing and dividing cells (*biograins*): interesting application of granular physics

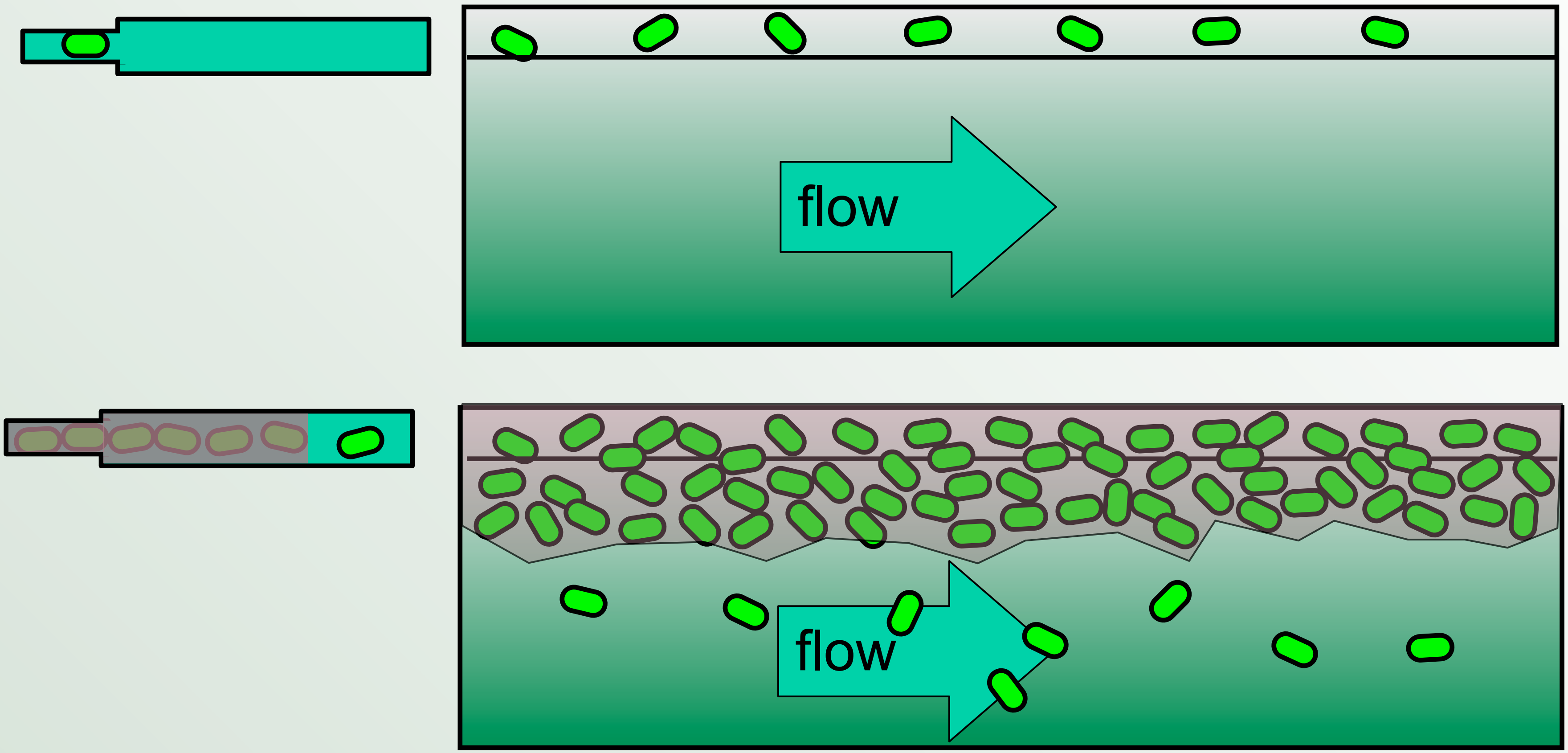
Publications

- D.Volfson, S. Cookson, J. Hasty, L. S.Tsimring, Biomechanical ordering of dense bacterial populations, Proc. Natl. Acad. Sci. USA, **105**, no. 40, 15346-15351 (2008)
- W. Mather, O. Mondragón-Palomino, T. Danino, J. Hasty L. S. Tsimring. Streaming instability in growing cell populations, Phys. Rev. Lett., **104**, 208101 (2010)
- D. Boyer, W. Mather, O. Mondragón-Palomino, S. Orozco-Fuentes, T. Danino, J. Hasty, L. S. Tsimring. Buckling instability in ordered bacterial colonies. Phys. Biol., **8,** 026008 (2011)

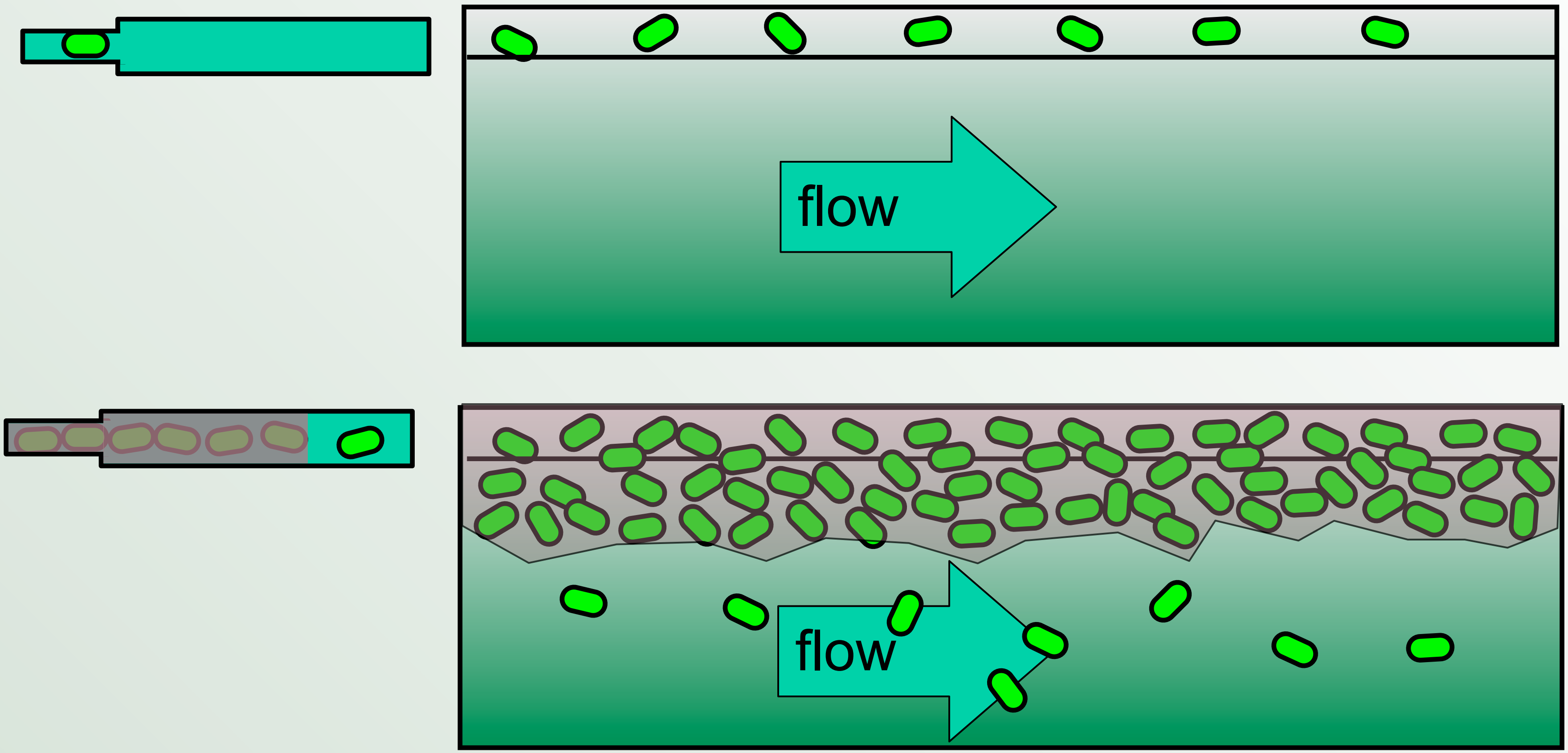
Future work: “real” biofilms



Future work: “real” biofilms



Future work: "real" biofilms



- track cell growth and movement
- measure mechanical properties of EPS (periodic flow)
- vary flow parameters (shear, temperature, chemicals)
- track gene expression *in situ*

(*E.coli*) biofilms are important!

Spanish MEP Francisco Sosa-Wagner holds a cucumber during a debate in the European Parliament on the recent outbreak of E.coli poisoning in Germany.