Lattice Boltzmann simulations of artificial morphogenesis in tissue engineering systems

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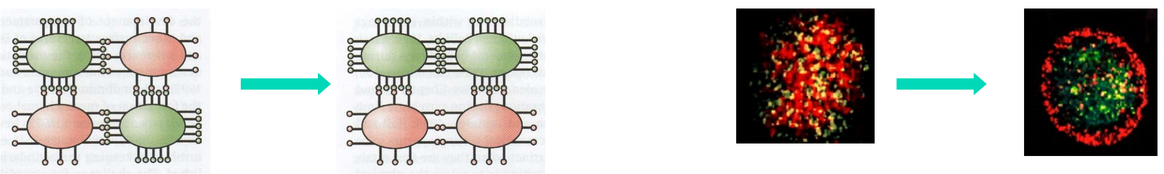
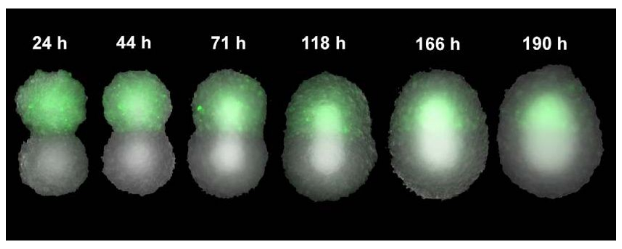
Differential Adhesion Hypothesis (DAH)[1]:

cells seek partners to interact with



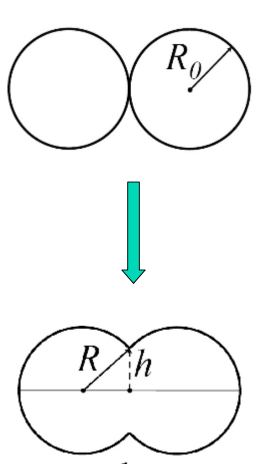
Tissue fusion is essential in developmental biology and tissue engineering

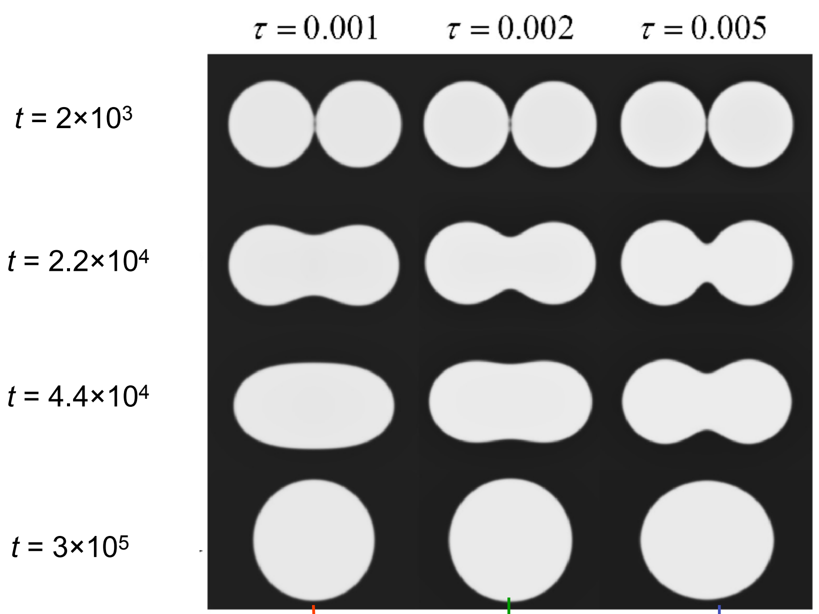


In vitro, aggregates of Chinese Hamster Ovary (CHO) cells fuse [2]

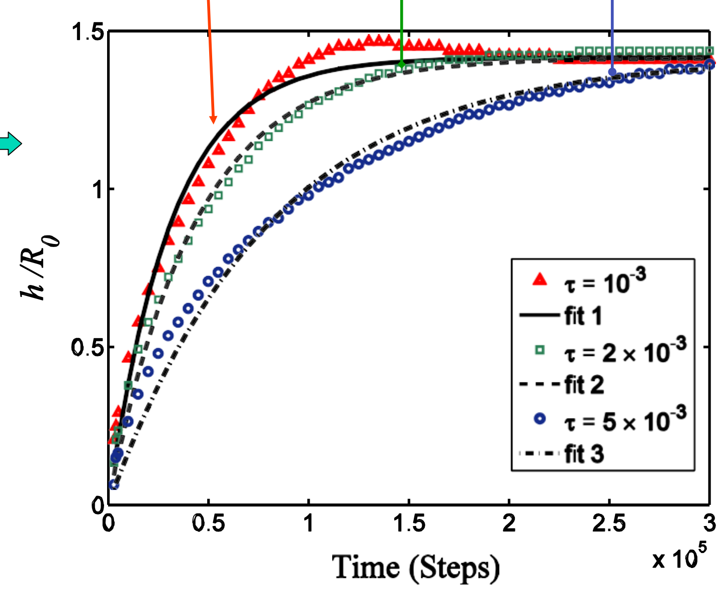
Lattice Boltzmann (LB) simulations of droplet fusion[4]:

the contact area describes the rate of fusion





$$\frac{h}{R_0} = \sqrt{2}\left[1 - \exp\left(-\frac{t}{t_f}\right)\right]$$



Lattice Boltzmann model using flux limiters[3] (for two species)

$$f_{i,j}^{\sigma,n+1} = f_{i,j}^{\sigma,n} - CFL^{\sigma}\left[F_{i,j+1/2}^{\sigma,n} - F_{i,j-1/2}^{\sigma,n}\right] - \frac{1}{\tau^{\sigma}}\left[f_i^{\sigma} - f_i^{\sigma,eq}\right] + \frac{\mathbf{F}^{\sigma}(\mathbf{r},t)}{m^{\sigma}\chi(c^{\sigma})^2}\cdot\left[\mathbf{e}_i^{\sigma} - \mathbf{u}(\mathbf{r},t)\right] f_i^{\sigma,eq}$$

BGK collision term

Force term

$$\mathbf{F}^{\sigma} = -\sum_{\lambda}\omega^{\sigma\lambda}\nabla X^{\lambda} + \kappa\nabla(\nabla^2 X^{\lambda}), \qquad X^{\sigma}(\mathbf{r},t) = \frac{n^{\sigma}}{n^0 + n^1}$$

$$F_{i,j+1/2}^{\sigma,n} = f_{i,j}^{\sigma,n} + \frac{1}{2}\left(1 - CFL^{\sigma}\right)\left[f_{i,j+1}^{\sigma,n} - f_{i,j}^{\sigma,n}\right]\psi(\theta_{i,j}^{\sigma,n})$$

Flux limiter terms

$$F_{i,j-1/2}^{\sigma,n} = F_{i,(j-1)+1/2}^{\sigma,n} = f_{i,j-1}^{\sigma,n} + \frac{1}{2}\left(1 - CFL^{\sigma}\right)\left[f_{i,j}^{\sigma,n} - f_{i,j-1}^{\sigma,n}\right]\psi(\theta_{i,j-1}^{\sigma,n})$$

MCD flux limiter scheme

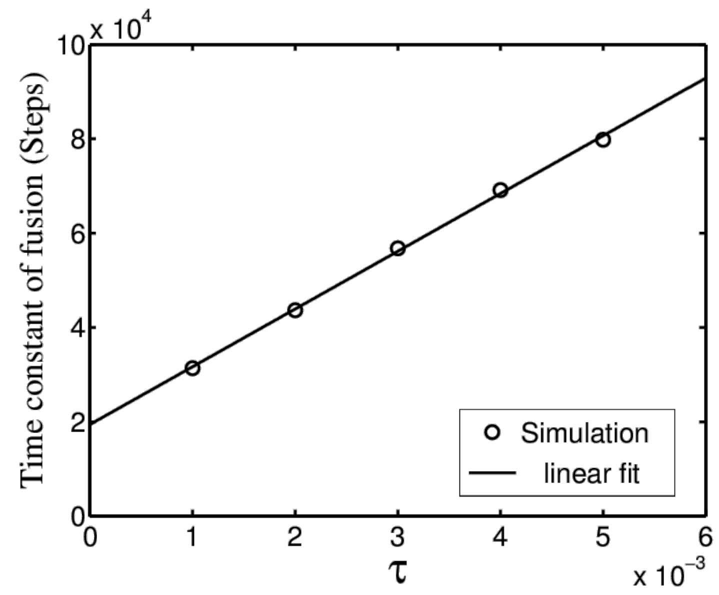
$$\psi(\theta_{i,j}^{\sigma,n}) = \begin{cases} 0 & , \theta_{i,j}^{\sigma,n} \le 0 \\ \frac{2\theta_{i,j}^{\sigma,n}}{1+\theta_{i,j}^{\sigma,n}} & , 0 \le \theta_{i,j}^{\sigma,n} \le \frac{1}{3} \\ \frac{1+\theta_{i,j}^{\sigma,n}}{2} & , \frac{1}{3} \le \theta_{i,j}^{\sigma,n} \le 3 \\ 2 & , 3 \le \theta_{i,j}^{\sigma,n} \end{cases} \qquad \theta_{i,j}^{\sigma,n} = \frac{f_{i,j}^{\sigma,n} - f_{i,j-1}^{\sigma,n}}{f_{i,j+1}^{\sigma,n} - f_{i,j}^{\sigma,n}}.$$

The time constant of fusion is proportional to the relaxation time and should be set in relation with the known values of viscosity and surface tension [4]

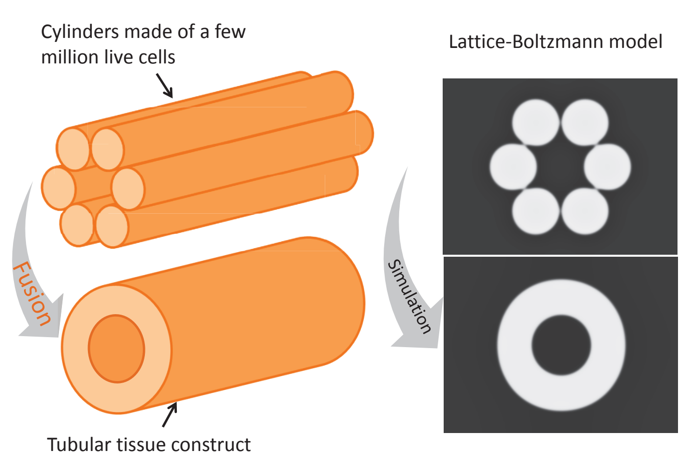
$$t_f \propto \frac{\eta}{\gamma}R_0$$

$$\frac{\eta}{\gamma} = \frac{\eta_0}{\gamma_0}(1 + b\tau)$$

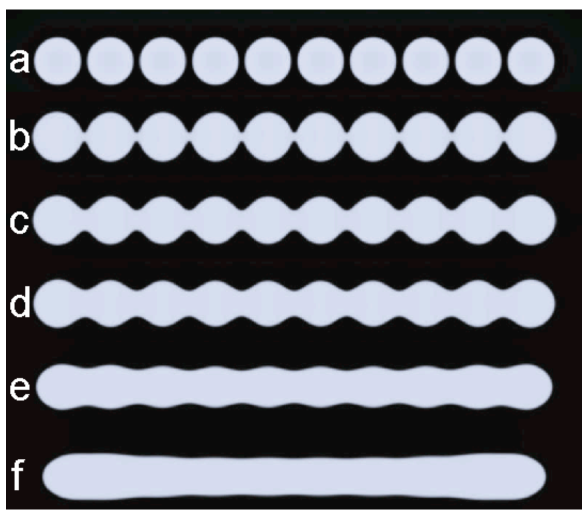
$$\tau' = \frac{\frac{\eta'}{\gamma'}}{\frac{\eta}{\gamma}}\tau + \frac{1}{b}\left(\frac{\frac{\eta'}{\gamma'}}{\frac{\eta}{\gamma}} - 1\right)$$

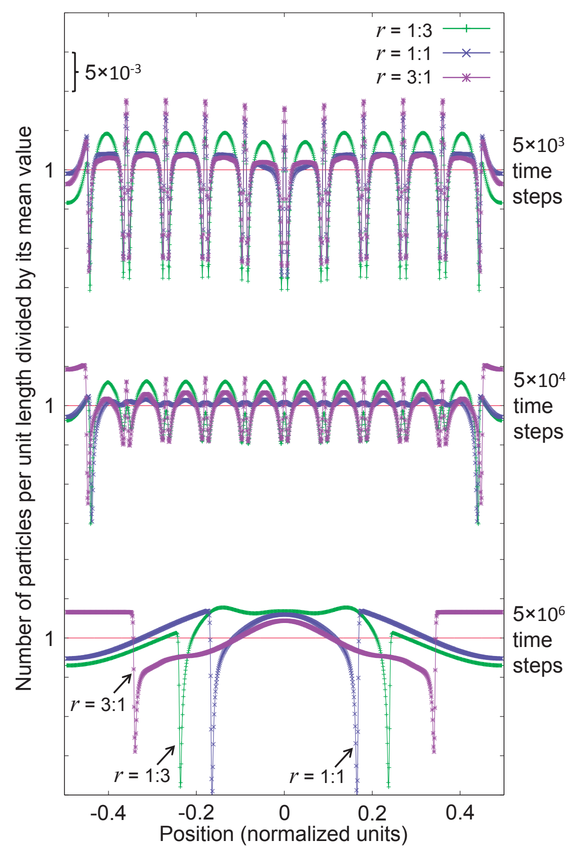


Cell cylinder printing[5] vs. LB simulations[6]



LB simulation time step corresponds to about 5.184 seconds in experiment.

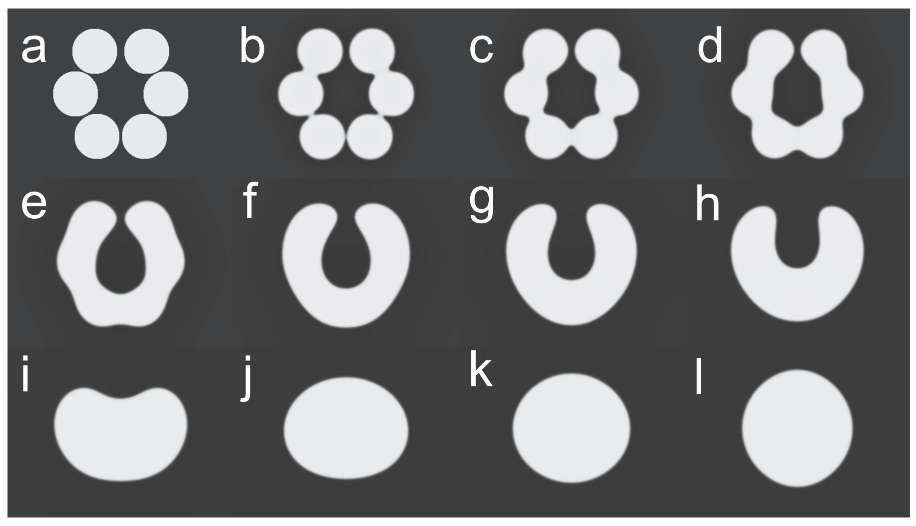




Perspectives

- Viscoelastic behavior;
- Cell division and cell death.

How does a printing defect evolve?[6]



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