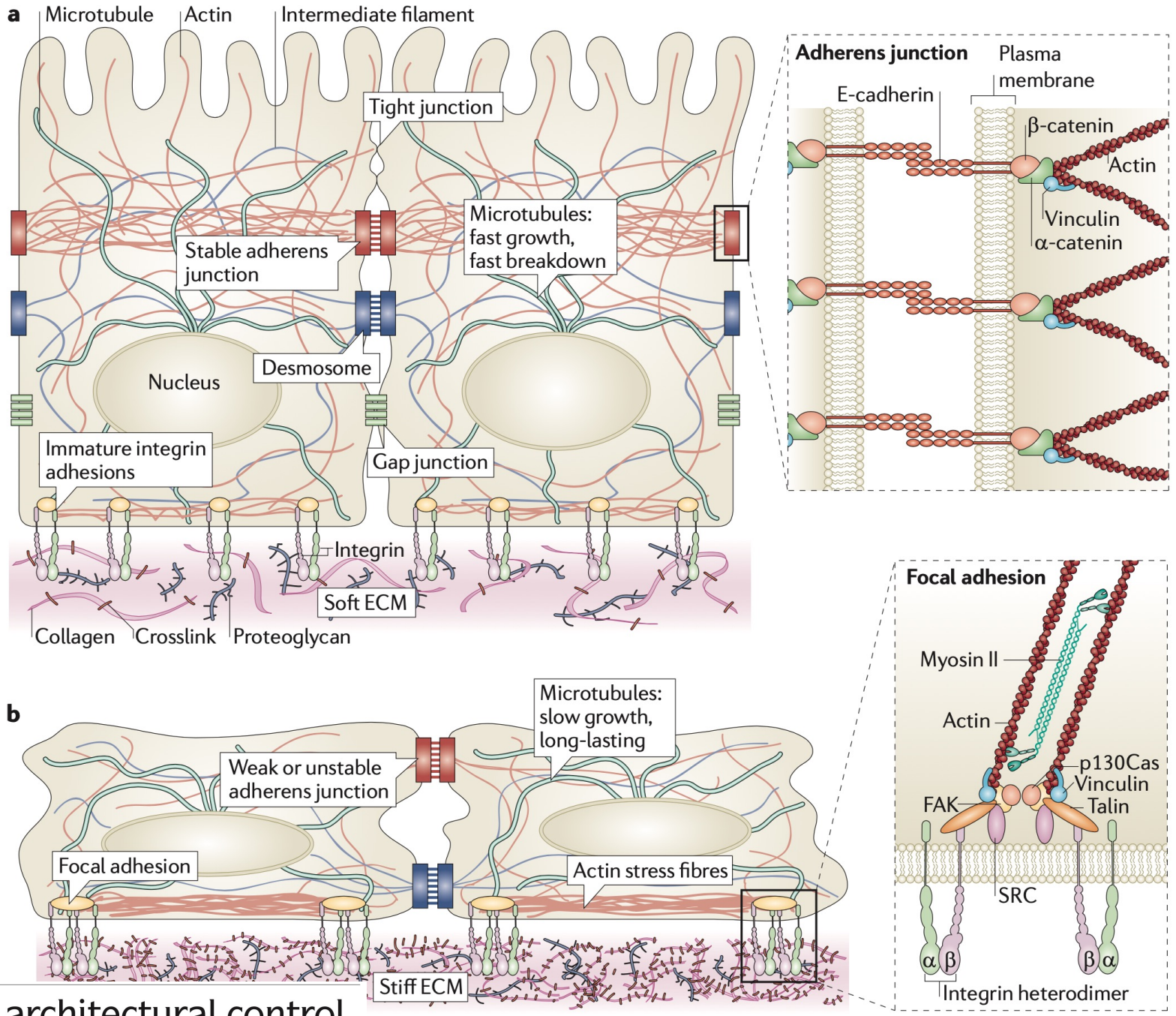
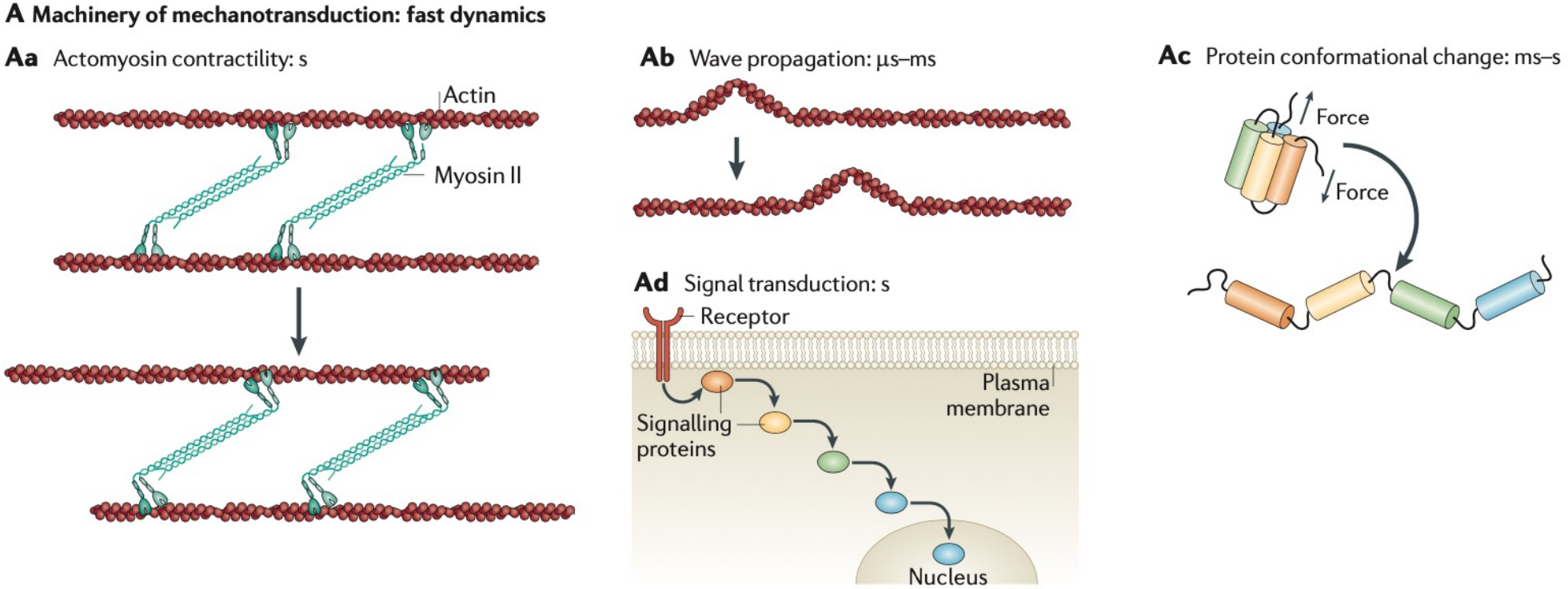
Mechanobiology, adhesion and models

Mechanotransduction: functional link between the sensing of mechanical cues and the subsequent biochemical response



Balancing forces: architectural control of mechanotransduction

Christopher C. DuFort, Matthew J. Paszek* and Valerie M. Weaver*‡*



Balancing forces: architectural control of mechanotransduction

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Focal adhesions

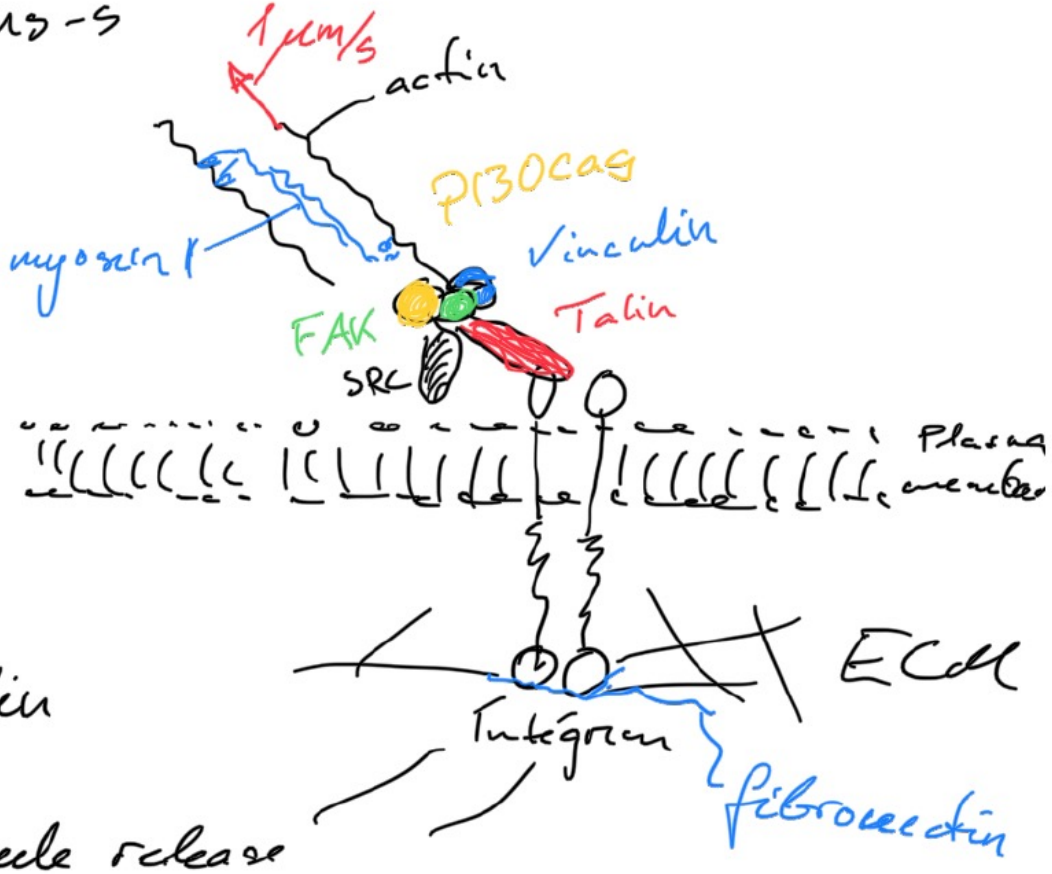
$\tau = ms - s$

Protein switches conformation change when forced

- Integrin
- P130cas
- Talin

Talin : unfolds => reveal binding sites

grow when force increases ⇐
- => binds vinculin
- => more integrins
- => signal molecule release

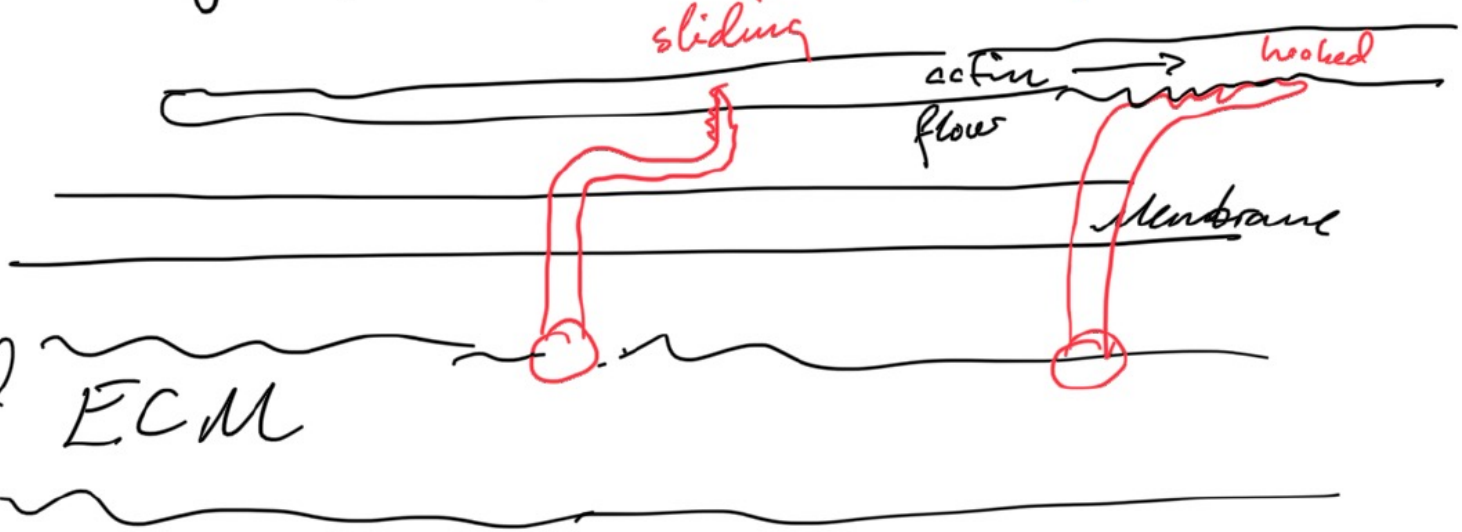


Other mechanisms

Forces → changed intermolecular distances → altered cellular function

Ref to Bershadsky, Kozlov, Geiger 2006 (400 citing articles)

Two state protein unit



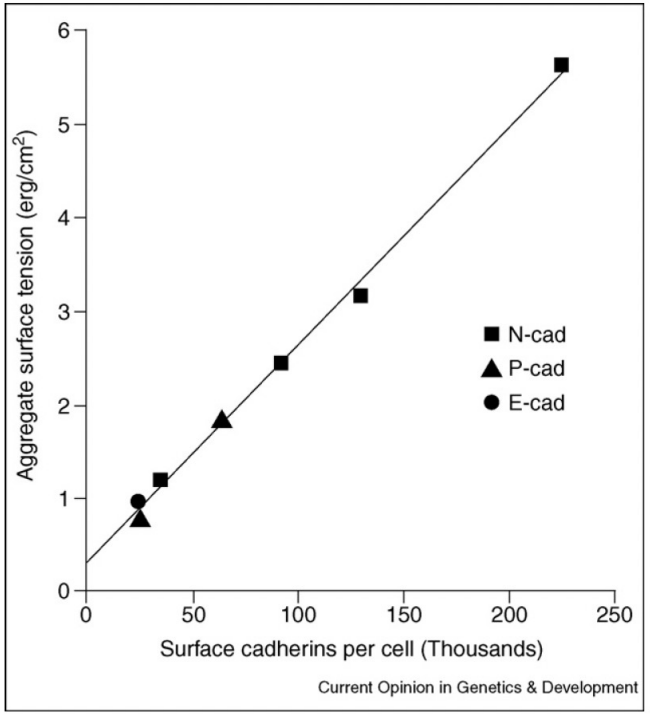
stress-induced flip

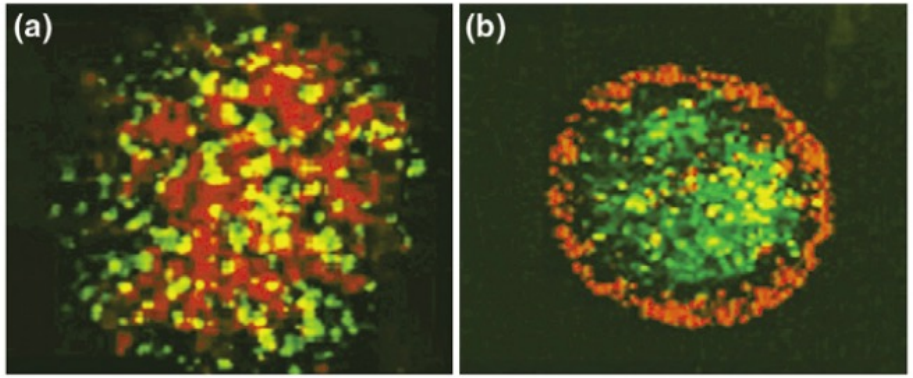
$$\Rightarrow \quad p = \frac{1}{1 + e^{-(F - f\Delta z)/kT}}$$

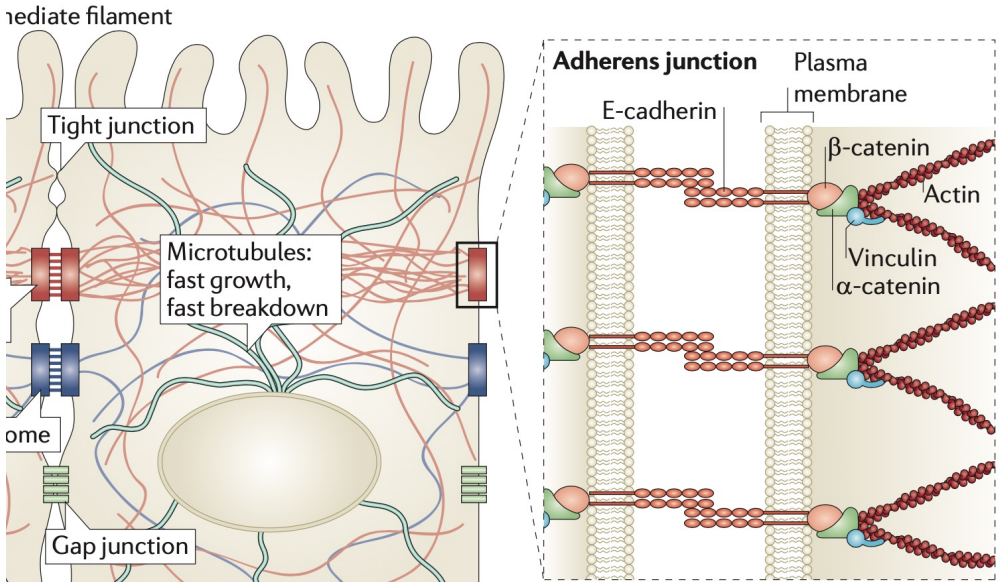
There is still a Δz !

Differential adhesion

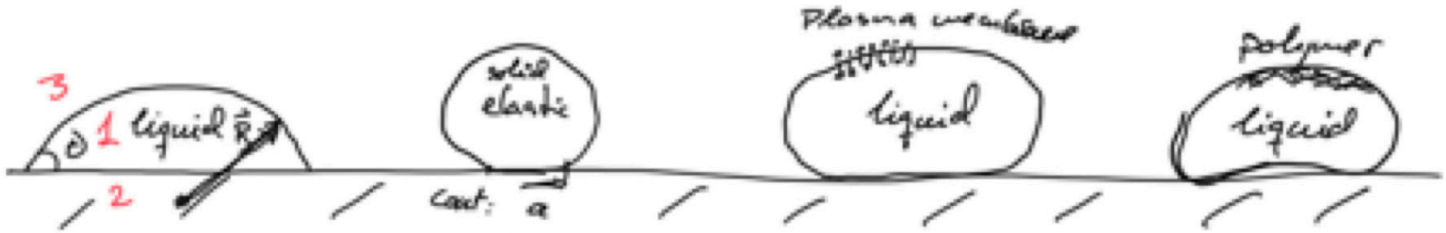
- Spreading of one embryonic tissue over another
- sorting of cells
- formation of intertissue boundaries







Vesicles



only surface energy | surf energy + solid elast. | surf en. bending energy | surf. en. bend + stretch energy

Young-Laplace equation $\Delta p = -\gamma H = -\gamma\left(\frac{1}{R_1} + \frac{1}{R_2}\right)$ → mean curvature

Surface energy $\gamma = \frac{W}{\Delta A}$ $\left(= \frac{F}{2L}\right.$ = surface tension$\left.\right)$

Young's law: $\cos\theta = \frac{\gamma_{23} - \gamma_{12}}{\gamma_{13}}$

Force balance

Elastic deformation counteracts adhesion energy gain W:

contact radius a: $a^3 = \frac{9\pi(1-\nu^2)}{2E} R^2 W$ JKR theory

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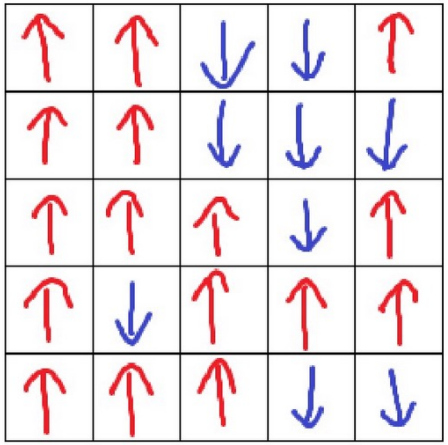
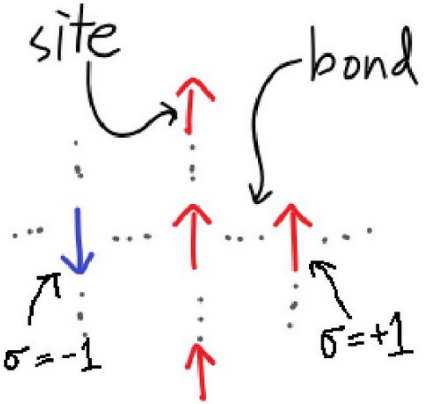
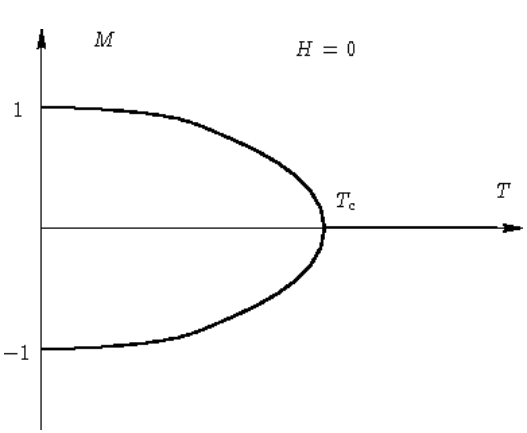
Bending energy $U_b = 2\kappa \int H^2 dA$ κ - bending rigidity

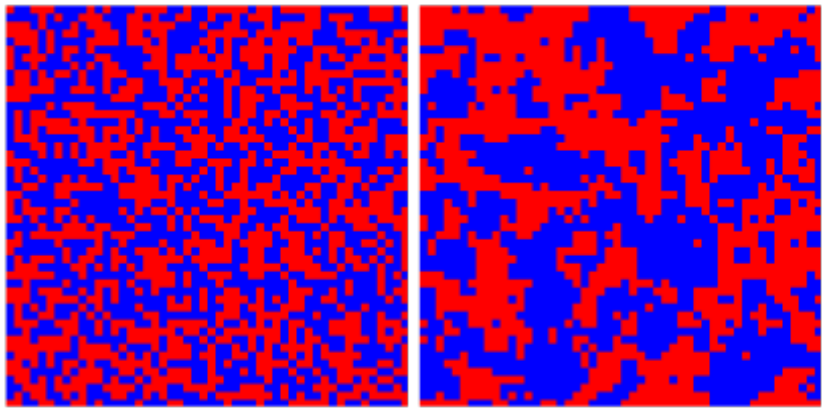
Biological bilipid membranes: $\kappa = 20kT$

Ising model

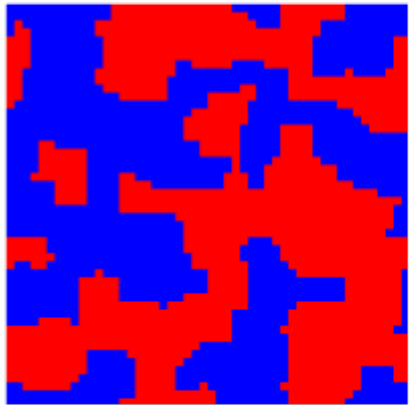






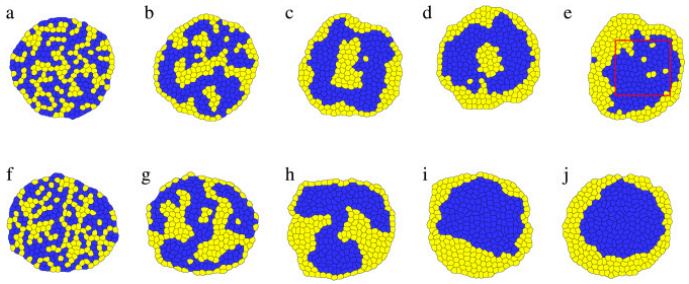


$T \gg T_C$ $T = T_C$

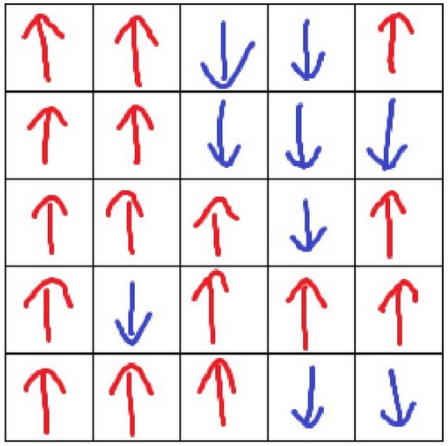


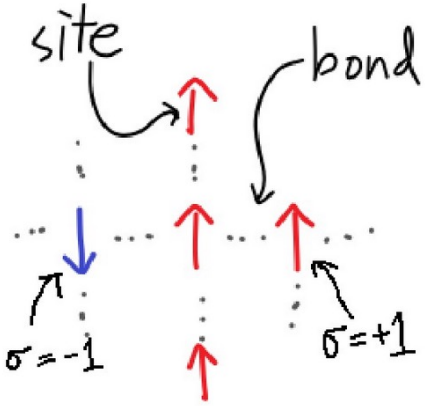
$T \ll T_C$

=> Cellular Potts model



Ising model





- Atoms sit on a lattice
- Atoms have magnetic spins $\sigma = \pm 1$ (up/down)
- Spins interact with nearest neighbour

$$H(\sigma) = -J \sum_{i,j} \sigma_i \sigma_j$$

- Spins interact with imposed magnetic field

$$H(\sigma) = -J \sum_{i,j} \sigma_i \sigma_j - h\mu \sum_{i} \sigma_i$$

J – spin-spin interaction, $[J]$=J
h – external magnetic field
μ – magnetic moment

Ising model, phase transitions

$$H(\sigma) = -J \sum_{i,j} \sigma_i \sigma_j - h\mu \sum_i \sigma_i$$

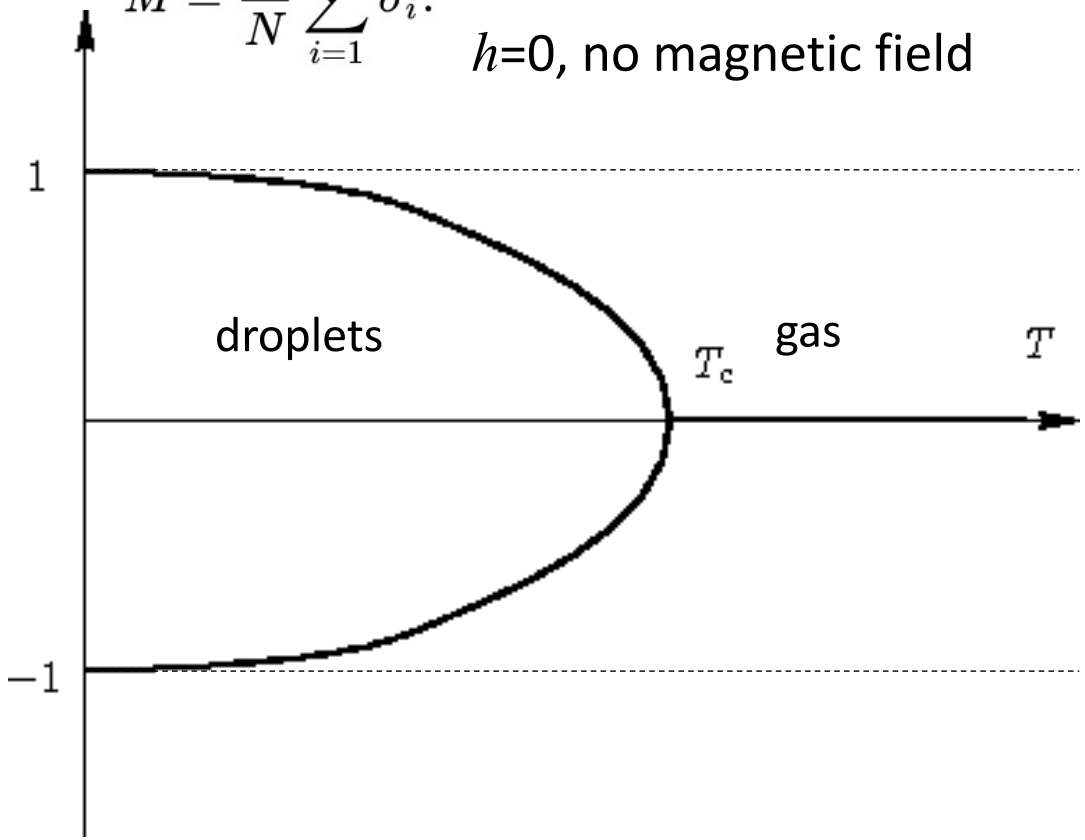
$$M = \frac{1}{N} \sum_{i=1}^{N} \sigma_i .$$

h=0, no magnetic field

.

$$P_\beta(\sigma) = \frac{e^{-\beta H(\sigma)}}{Z_\beta},$$

$$Z_\beta = \sum_\sigma e^{-\beta H(\sigma)}$$



Onsager's Nobel prize:
Solved 2D Ising Model analytically

Monte Carlo

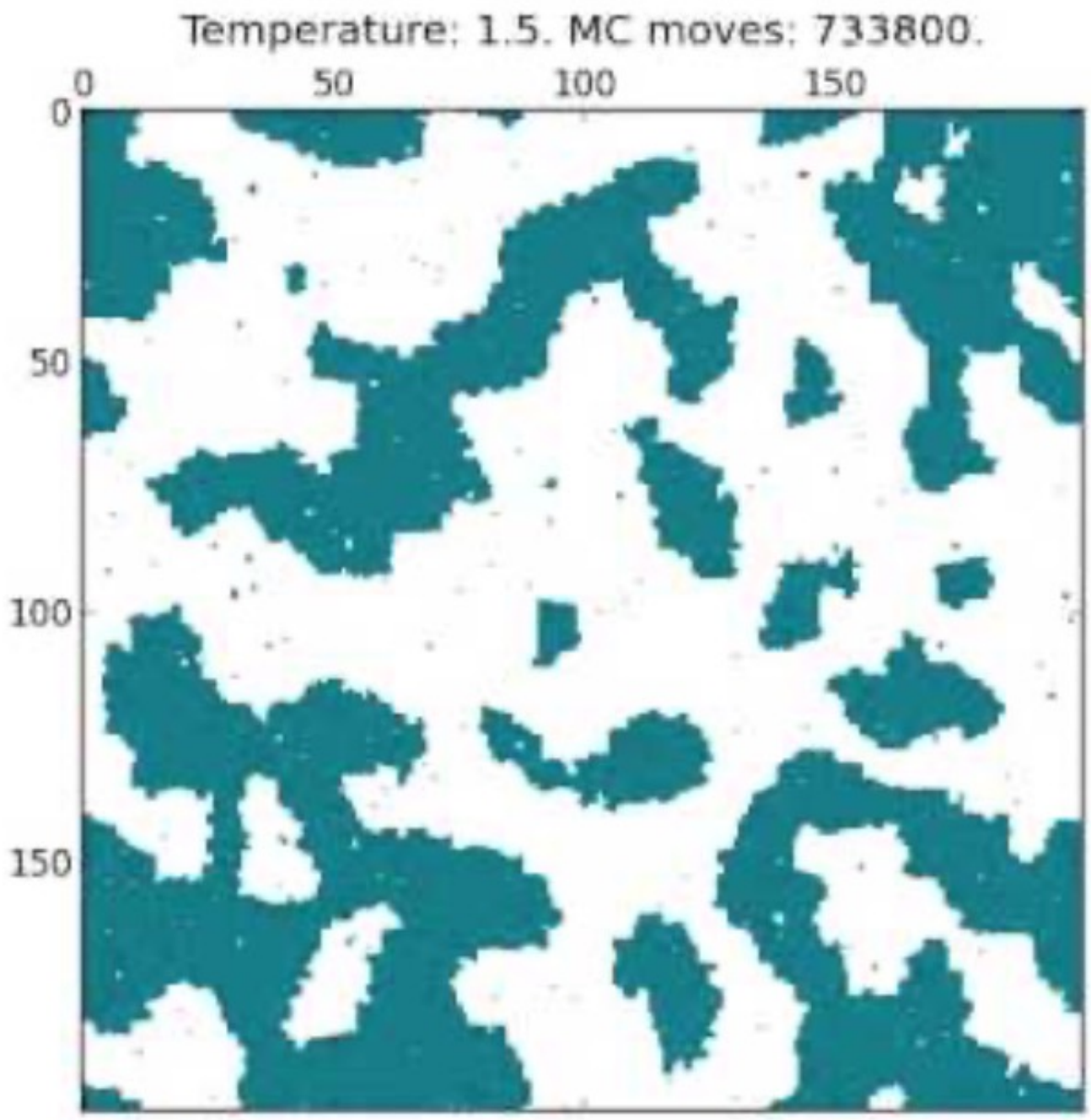
1. Choose a lattice site at random. We call this the *target site*, which we wil denote $\vec{i}_{\text{target}}$ and its spin, the *target spin*, which we will denote σ_{target}.
2. Pick any value of spin at random. We call this spin the *trial spin* and denote it σ_{trial}.
3. Calculate the current configuration energy, $\mathcal{H}_{\text{initial}}$, and the energy of the configuration if the target spin were changed to the trial spin value, $\mathcal{H}_{\text{final}}$.
4. Calculate the change this substitution would cause in the total energy, *i.e.*

$$\Delta\mathcal{H} = \mathcal{H}_{\text{final}} - \mathcal{H}_{\text{initial}}, \tag{8}$$

5. Accept this change (*i.e.* really change the spin value at the lattice site) with probability:

$$p(\sigma(\vec{i}_{\text{target}}) = \sigma_{\text{target}} \rightarrow \sigma(\vec{i}_{\text{target}}) = \sigma_{\text{trial}}) = \begin{cases} 1 & \text{if } \Delta\mathcal{H} < 0, \\ e^{-\Delta\mathcal{H}/T} & \text{if } \Delta\mathcal{H} > 0. \end{cases} \tag{9}$$

   Steps 1 through 5 together are called a *spin-copy attempt.*
6. Go to 1.


Temperature: 1.5. MC moves: 733800.
0
50
100
150
0
50
100
150

Ising

2.1.3. Summary. The Ising model contains two key ideas that carry forward to the GGH model:

1. The energy of mismatched links between neighboring spins on a lattice represents the energy per unit length of the boundaries between domains.
2. A temperature or *fluctuation amplitude* determines the probability of a configuration.
3. Dynamics and roughness increase with T.

Potts model

$$\mathcal{H}_{\text{Potts}} = J \sum_{(\vec{i},\vec{j})\ \text{neighbors}} (1 - \delta(\sigma(\vec{i}), \sigma(\vec{j}))), \tag{4}$$

where $\delta(x, y) = 0$ if $x \neq y$ and 1 if $x = y$. We denote the number of possible spin values by q. The Potts model has ferromagnetic and other phase transitions [6, 71].

2.2.1. Summary. The Potts model contains two key idea for biological simulations:

1. Individual domains can have individual spins (which in CPM and GGH simulations we refer to as *cell indices*.)
2. Domains have a boundary energy that can be used to model adhesivity.

Direct application to grain boundaries

Foams: not direct

Cellular Potts model

$$\mathcal{H}_{\mathrm{CPM}} = \sum_{(\vec{i},\vec{j})\ \mathrm{neighbors}} J(\tau(\sigma(\vec{i})),\tau(\sigma(\vec{j})))(1-\delta(\sigma(\vec{i}),\sigma(\vec{j})))$$

$$+\sum_{\sigma}\lambda_{\mathrm{Vol}}(\tau)(v(\sigma)-V_{\mathrm{t}}(\tau(\sigma)))^2,$$

cell index	σ
cell type	$\tau(\sigma)$
lattice sites	$\vec{i},\vec{j}$
volume of cell	$v(\sigma)$
target volume	V
strength of volume constraint	λ_{Vol}