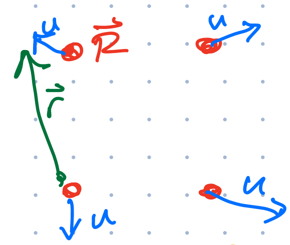
Boulder Summer School
Manning lectures on emergent mechanics in tissues
July 15-17, 2024

Lecture 1

How to determine if a material is rigid or floppy?

Crystalline materials
(Ashcroft & Mermin Chapter 22)



lattice points R

actual location $\vec{r}(\vec{R}) = \vec{R} + \vec{u}(\vec{R})$

recall Mounita Das lecture 2 from week 1

quadratic in u

energy $\mathcal{U} \cong \frac{1}{2} \sum_{\substack{R'R \\ \mu,\nu}} \vec{u}_\mu(\vec{R}) D_{\mu\nu}(\vec{R}-\vec{R}') \vec{u}_\nu(\vec{R}')$ + higher order terms

$\mathcal{U}$ not constant

dynamical matrix

¿ why isn't there a force that is linear in u?

Because of the symmetry of the lattice, can take a fourier transform, e.g. $u \propto e^{i(kna - \omega t)}$

normal mode (eigenvector)

$$D(k)\, \epsilon_s(\vec{k}) = \lambda_s \epsilon_s(\vec{k})$$

$3b \times 3b$ matrix
b = # of basis points in the crystal

wavenumbers

eigenvalue

$$\omega_s(k) = \sqrt{\frac{\lambda_s(k)}{M}}$$

This equation says that D is diagonalizable, with eigenvalues that are positive.

The fact that $\lambda \geq 0$ means any small perturbation u results in a restoring force that drives the system back towards the lattice.

which can be written as a sum of $\epsilon_s(\vec{k})$

This means the system is rigid → there are no perturbations u_i to the lattice that cost zero energy.

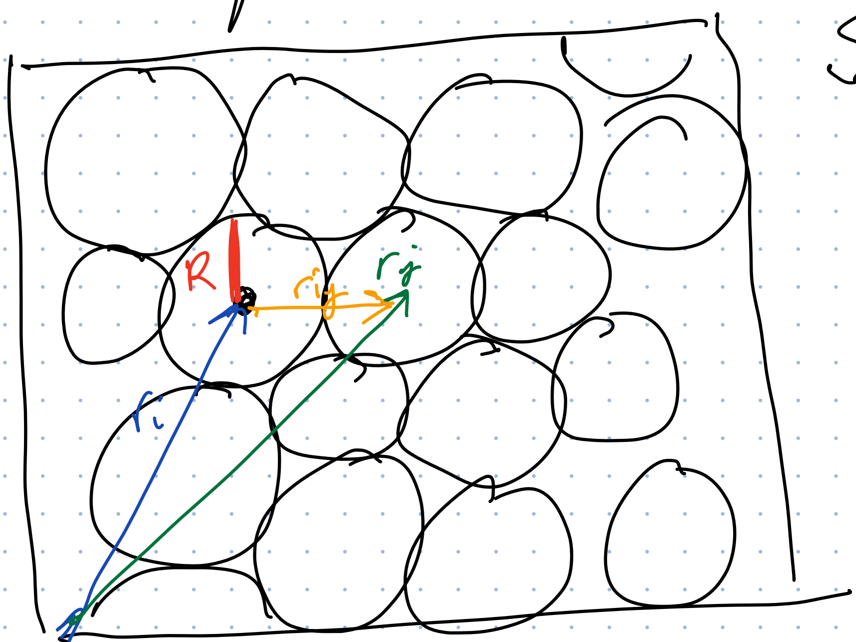
What about disordered materials?

Examples?? Glasses, Polymers, cells, piles of ants or bees
Granular materials, fibers

Moumita's lectures

finite temperature
Glasses are really challenging, we will reserve discussion for later.

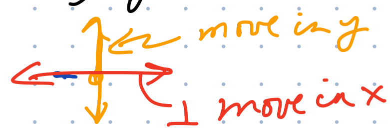
But $T=0$ limit of repulsive spheres is simpler to understand.



Setup:
N particles in d dimensions of radius R

$\vec{r}_i$: location of center of particle i

There are d degrees of freedom ~~for~~ per particle, e.g. in 2d:



2-body interaction: let $\vec{r}_{ij} = \vec{r}_i - \vec{r}_j$

$$F_{ij} = \begin{cases} -k\,(2R - r_{ij})^{\alpha}\,\hat{r}_{ij} & \text{if } r < 2R \\ + k\,(l - l_0) & \\ 0 & \text{o.w.} \end{cases} \qquad \alpha = 1, \tfrac{3}{2}$$

$\rightarrow$ one-sided spring with rest length $l_0 = 2R$

Recall from Moumita's lectures in Week 1 (Lecture 1)

$\therefore$ Each contact between a pair of particles introduces a constraint on the motion of these two particles e.g. it costs energy to move them closer together

let z = number of contacts per particle

then there are $\frac{z}{2}$ constraints (because each constraint is shared by 2 particles)

So, there are $\frac{z}{2}$ constraints per particle

and d degrees of freedom per particle

Should be come rigid when equal

$$\frac{z_c}{2} = d \Rightarrow z_c = 2d$$

(Works!)

Called "isostaticity" from "constraint counting"

Now let's understand why it works

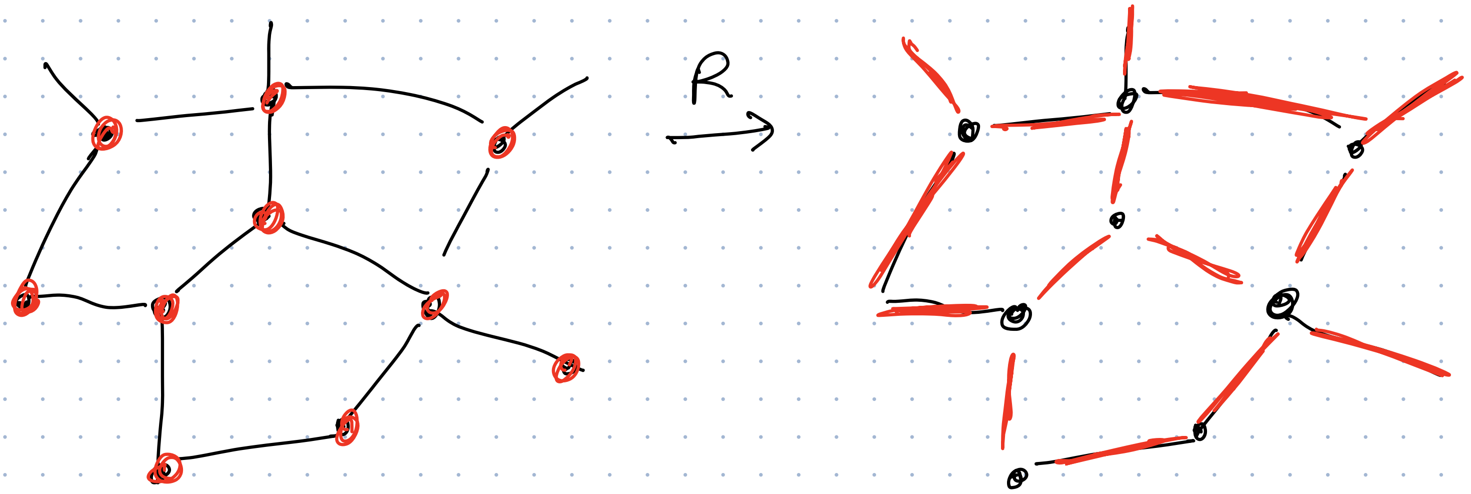
If we have a network where the interaction energy is a function of a set of constraints f_α, e.g.

$$F = -k(l - l_0) \Leftrightarrow U = \sum_\alpha \frac{k}{2} \underbrace{(l_\alpha - l_0)}_{\text{constraint } f_\alpha \text{ on bond } \alpha \text{ in disordered network}}{}^2$$

Could be a spring network for ECM

contact network for ~~cells~~ non-confluent cells

vertex model for confluent cells



mapping from configuration space to constraint space f_α, parametrized by bond vectors

$\vec{x}_i$ ← index the vertices $\qquad$ $\vec{\ell}_\alpha$ ← index constraints

How many $x_{i\mu}$ ← dimension $\qquad$ How many constraints?

Nd $\qquad$ M

Ultimately, we want to know if it is possible to change the configuration without ↑ energy

→ this means the system is floppy

variation $\delta\mathcal{U} = 0$ for <u>any</u> change in $\vec{x}_i$

but since $\mathcal{U}$ is a function of the f_α, it <u>usually</u> suffices to check whether there are variations to any of the f_α that cost zero energy.

This is called <u>structural rigidity</u>

We want to know how a change to the $\vec{x}_i$ changes the constraints f_α:

$$\delta f_\alpha = \sum_{i\mu} \frac{\partial f_\alpha}{\partial x_{i\mu}} \delta x_{i\mu} + \text{higher order terms}$$

$\Rightarrow$ $\exists\ \delta x_{i\mu}$ s.t. $\delta f_\alpha = 0$?

Note that this object: $R_{\alpha i\mu} \equiv \dfrac{\partial f_\alpha}{\partial x_{i\mu}}$

called the <u>rigidity matrix</u>

is a map from configuration space to constraint space:
it tells you how changes to $\vec{x}_{i\mu}$ alter the bonds:

$$\underbrace{M\text{ rows}\left\{\begin{bmatrix} \frac{\partial f_1}{\partial x_{1x}} & \frac{\partial f_1}{\partial x_{1y}} & \frac{\partial f_1}{\partial x_{2x}} & \cdots & \\ \frac{\partial f_2}{\partial x_{1x}} & \ddots & & & \\ & & & \ddots & \\ \frac{\partial f_M}{\partial x_{1x}} & & & & \frac{\partial f_M}{\partial x_{Ny}} \end{bmatrix}\right.}_{Nd\text{ cols}}^{\overleftrightarrow{R}} \overbrace{\left.\begin{bmatrix} \delta x_{1x} \\ \delta x_{1y} \\ \vdots \\ \delta x_{Nx} \\ \delta x_{Ny} \end{bmatrix}\right\} Nd}^{\vec{\delta x}}$$

R is rectangular

it has M rows and N columns

Are there a set of displacements $\vec{\delta x}$ that don't change any of the constraints?

$$\overleftrightarrow{R} \cdot \vec{\delta x} = 0 \iff \exists\, \vec{\delta x} \text{ in the right null space of } R$$

These $\vec{\delta x}$ are called linear zero modes (LZM)

Let $\boxed{N_0}$ be the number of independent LZM

We could also consider the map that takes us from constraint space back to configuration space, R^T:

$\rightarrow$ $\exists$ a set of perturbations to the bonds (e.g. tensions) that do not cause changes to the constraints?

$\vec{\sigma}$

$\frac{1}{\delta f_\alpha}$

$$0 = \overleftrightarrow{R}^T \cdot \vec{\sigma} = \underbrace{Nd\left\{\begin{bmatrix} \frac{\partial f_1}{\partial x_{1x}} & & \frac{\partial f_M}{\partial x_1} \\ & & \\ \frac{\partial f_1}{\partial x_{Ny}} & & \end{bmatrix}\right.}_{M}^{R^T} \overbrace{\left.\begin{bmatrix} \sigma_1 \\ \vdots \\ \sigma_M \end{bmatrix}\right\} M}^{\vec{\sigma}}$$

These $\vec{\sigma}$ are called states of self stress

They are sets of tensions on the bonds that don't move any of the vertices.

They are in the right null space of map R^T

or equivalently in the left null space of R

$$0 = \vec{\sigma} \cdot \tilde{R}$$

Let $\boxed{N_{ss}}$ be the number of independent states of self stress.

Now we can use the rank nullity theorem on $\tilde{R}$ to derive a nice result:

$$\underbrace{\text{rank}(R) + \text{null}(R)}_{} = \underbrace{\text{dim}(R)}_{N_d} \qquad \underbrace{\text{dim}(R^T)}_{M} = \text{rank}(R^T) + \text{null}(R^T)$$

N_0 $\qquad$ $+ N_{ss}$?

$$\text{rank}(R) = \text{rank}(R^T) \Rightarrow \text{dim}(R) - \text{null}(R) = \text{dim}(R^T) - \text{null}(R^T)$$

$$N_d - N_0 = M - N_{ss}$$

$$\Rightarrow \boxed{\boxed{N_0} = N_d - M + \boxed{N_{ss}}}$$ Maxwell-Calladine constraint counting

Examples: ① when do jamming particles become rigid? $\quad N_0 = 0$ (rigid)

$$M = \frac{Nz}{2}$$

$$\cancel{N_0}^{\,0} = N_d - \frac{Nz}{2} + \cancel{N_{ss}}^{\,0} \qquad N_{ss} = 0 \text{ at jamming}$$

$$\text{when } N_d = \frac{N z_c}{2}$$

$z < z_c$ "underconstrained"

$z > z_c$ "overconstrained"

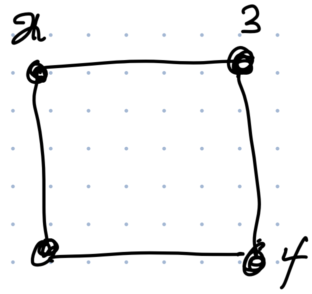
$$\Rightarrow \boxed{z_c = 2d}$$

So: Maxwell-Calladine constraint counting + isostaticity is considering first order perturbations to constraints.

Called first-order rigidity.

Example (2)

Lubensky 2015



4 bar linkage in 2d

$Nd = (4)(2) = 8$

$M = 4$

$N_0 = 8 - 4 = 4$

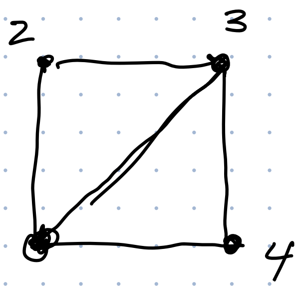
¿ what are these zero modes?

3 rigid body motions

+ 1 non-trivial floppy mode

[Called "underconstrained"]

Example (3)



5 bar linkage in 2d

$Nd = 8$

$M = 5$

$N_0 = 8 - 5 = 3$

↑ only rigid body rotations

No non-trivial zero modes

⇒ This is not floppy

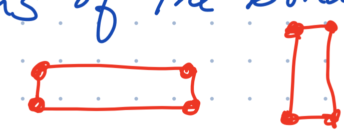
It is rigid.

Lecture 2

Example (4) 4-bar linkage revisted

Note that none of what we did above depended on the rest lengths of the bonds/bars.

So we could have considered



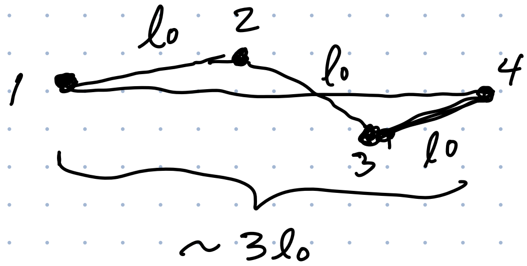
lots of geometries at fixed topology

positions of vertices / lengths of bonds

connectivity of the network

"under constrained"

So, we could consider a special case where

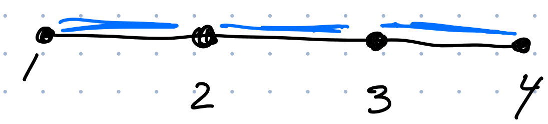


we stretch out the bond between 1 and 4.

Let's choose the distance between 1 & 4 such that it is almost exactly 3 times the rest length of the other bars:

Then the square becomes almost flat.

If we make $\ell_{14} > 3\ell_0$ then the system is flat, and



none of the constraints are satisfied,

e.g $f_{12} > 0$, $f_{23} > 0$, $f_{34} > 0$

$(\ell_{12} > \ell_0)$

There is tension in all of the bonds, that doesn't change the vertex positions $\Rightarrow \exists$ a state of self

Constraint counting:

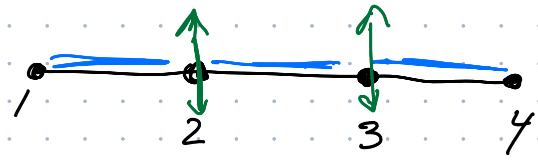
$$Nd = 8$$
$$M = 4$$
$$N_{ss} = 1$$

$N_0 = 8 - 4 + 1 = 5$ floppy modes

3 rigid body motions + 2 nontrivial zero modes?

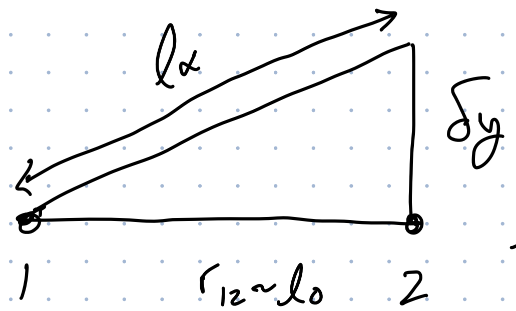
But the object should be rigid, $f_\alpha > 0$ and perturbations should cost energy!

Is this right?



Yes. This analysis only tells us about perturbations to 1st order in the constraints

$\exists$ 2 linear (LZM) zero modes that cost zero energy to first order.



for $\delta \ll l_0$

$$l_\alpha = \sqrt{r_{12}^2 + \delta y^2}$$

$$= r_{12}\sqrt{1 + \left(\frac{\delta y}{r_{12}}\right)^2}$$

$$= r_{12}\left(1 + \frac{1}{2}\left(\frac{\delta y}{r_{12}}\right)^2\right)$$

¿?

No term that is linear in δ!

$$\frac{\partial f_{12}}{\partial \delta y} = 0$$

(Rigidity matrix doesn't know about this cost.)

$\Rightarrow$ For this special geometry, we need to consider second-order perturbations to the constraints:

¿0 for a LZM?

$$\text{(☆)} \quad \delta f_\alpha = \cancel{\sum_{i\mu} \frac{\partial f_\alpha}{\partial x_{i\mu}} \delta x_{i\mu}} + \frac{1}{2} \sum_{i\mu, j\nu} \frac{\partial^2 f_\alpha}{\partial x_{i\mu} \partial x_{j\nu}} \delta x_{i\mu} \delta x_{j\nu}$$

if the only $\delta x_{i\mu}$ that satisfy ☆ are rigid body motions, then system is second-order rigid.

How to figure this out?

Kind of complicated, in all generality, but here we'll sketch out the idea:

Appendix A to Damavandi PRE 2021

For a $\mathcal{U}$ that is quadratic in some constraint

$$\mathcal{U} = \tfrac{1}{2} \sum_\alpha f_\alpha^2 , \quad \text{at an energy minimum?}$$

0 } because

$$\delta \mathcal{U} = \sum_{i\mu} \left(\cancel{\sum_\alpha f_\alpha \frac{\partial f_\alpha}{\partial x_{i\mu}}} \delta x_{i\mu} \right) + \sum_{i\mu} \sum_{j\nu} \underbrace{\frac{\partial^2 \mathcal{U}}{\partial x_{i\mu} \partial x_{j\nu}}}_{\text{our friend Dynamical matrix! } D} \delta x_{i\mu} \delta x_{j\nu}$$

$$+ \tfrac{1}{2} \sum_\alpha \left[\sum_{i\mu} \Big(\underbrace{\frac{\partial f_\alpha}{\partial x_{i\mu}}}_{\substack{R_{\alpha i\mu} \\ \text{rigidity matrix}}} \delta x_{i\mu} \Big)^2 + \sum_{i\mu, j\nu} f_\alpha \underbrace{\frac{\partial^2 f_\alpha}{\partial x_{i\mu} \partial x_{j\nu}}}_{P_{\alpha i\mu j\nu} \ \text{"pre-stress" matrix}} \delta x_{i\mu} \delta x_{j\nu} \right]$$

note: can compute shear modulus from D (more on Wed) ⟹ HW problem

$$D = \sum_\alpha R_\alpha^T R_\alpha + P_\alpha = R^T R + P$$

$$\Rightarrow \boxed{\delta \mathcal{U} = 0 \text{ to second order} \iff \overset{\text{LHS}}{P \cdot \vec{\delta x}} = \overset{\text{RHS}}{-R^T R \cdot \vec{\delta x}} \text{ for some } \vec{\delta x}}$$

- For many systems including spring networks and some vertex model i) ∃ only one state of self stress σ_α near the transition, for which the pre-stress matrix is ii) positive semi-definite

$$\text{so } \text{LHS} = \sum_{i\mu, j\nu} \sigma_\alpha \frac{\partial^2 f_\alpha}{\partial x_{i\mu} \partial x_{j\nu}} \delta x_{i\mu} \delta x_{j\nu} \geq 0$$

- But $\overset{\text{RHS}}{R^T R}$ is also positive semi-definite, as it is a sum of terms that are all ≥ 0 : $\sum_\alpha \left(\sum_{i\mu} \frac{\partial f_\alpha}{\partial x_{i\mu}} \delta x_{i\mu} \right)^2$
- So these two can only be equal when both sides are zero.

but RHS zero only for $\vec{\delta x}$ a LZM

$\Rightarrow$ For these systems where i) and ii) hold $\quad \delta U = 0 \Longleftrightarrow$

$$\boxed{\sum_{\alpha} \sum_{i\mu, j\nu} \sigma_\alpha \frac{\partial^2 f_\alpha}{\partial x_{i\mu}\,\partial x_{j\nu}}\, \delta x_{i\mu}\, \delta x_{j\nu} = 0 \quad \text{for } \vec{\delta x} \text{ a LZM}}$$

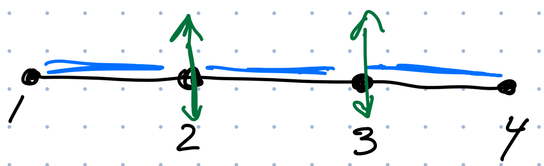
condition on linear zero mode so that it is also floppy to second order.

— OR —

$$\boxed{\vec{\delta x} \cdot \vec{P} \cdot \vec{\delta x} = 0}$$

Note: there are systems for which P is not positive semi-definite, and in general then this condition is not sufficient to prove floppiness.

So, going back to our example:



- $\exists$ a state of self-stress σ_α.
- our LZM is δy.

$$l_\alpha = r_{12} + \frac{1}{2}\frac{(\delta y)^2}{r_{12}}$$

$$\frac{\partial l_\alpha}{\partial(\delta y)} = \frac{(\delta y)}{r_{12}}$$

$$\frac{\partial^2 l_\alpha}{\partial(\delta y)^2} = \frac{1}{r_{12}} \neq 0$$

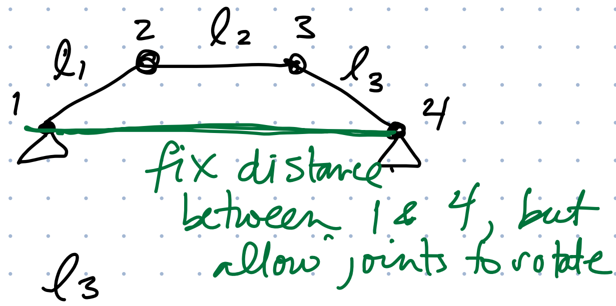
- $\displaystyle \frac{\partial^2 f_\alpha}{\partial(\delta y)^2} = \frac{\partial^2 l_\alpha}{\partial(\delta y)^2} \sim \frac{1}{r_{12}} \neq 0$

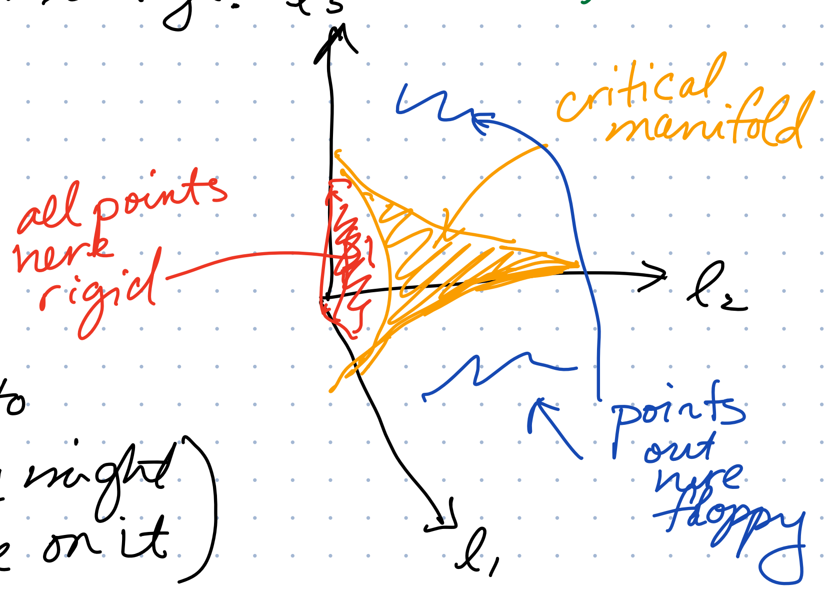
$\Rightarrow$ not floppy to second order.

$\therefore$ the system is rigid.

One might think that this is a special example, as this particular geometry won't happen generically.

But it turns out that rigid states are a finite region of the space for this example. To see this, its a little easier to plot the phase space with a 3-bar linkage.





In lecture 3, I'll talk more about the properties of this critical manifold and how one might use it to design stuff (or how biology might self-organize on it)

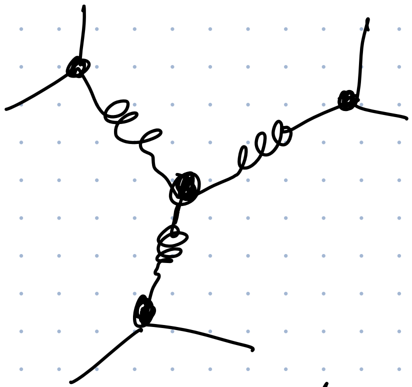
Key point: Not a special feature of this example.

very generic: a change in geometry of network can allow an underconstrained material to become rigid.

⇒ slides on fiber networks for Lecture 2

Examples: ① Underconstrained spring networks

$z < z_c$ in both 2D & 3D



- model for collagen networks
- typical branching connectivity is between 3 & 4 "underconstrained"
- $f_\alpha = \sqrt{k_\alpha}(l_\alpha - l_0)$, just as in our formulation above
- $\mathcal{U} = \frac{1}{2}\sum_\alpha' f_\alpha^2$
- We can either keep box fixed and shrink rest length l_0 or fix l_0 and grow size of the box "strain"

N_{DOF} : $N_{vertices}\, d$

M : $\frac{z}{2} N_{vertices}$ ← e.g. 3 in 2D

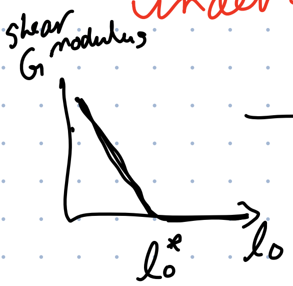
constraints M < N_{DOF}

$\frac{3}{2} N_v$ < $2N_v$

"underconstrained"

⇒ Find ∃ a critical l_0^* for $l_0 < l_0^*$ the system becomes rigid

⇒ Equivalently ∃ a critical size of the box or strain at which system becomes rigid



$$l_{\alpha\mu} = g_{\alpha i} X_{i\mu} + b_{\alpha\mu}$$

vector along bond; incidence matrix; coordinates of vertex i; encodes boundary conditions (fixed or periodic)

$$g_{\alpha i} = \begin{cases} 1 & \text{if vertex } i \text{ is at head of edge } \alpha \\ -1 & \text{" " tail} \\ 0 & \text{o.w.} \end{cases}$$

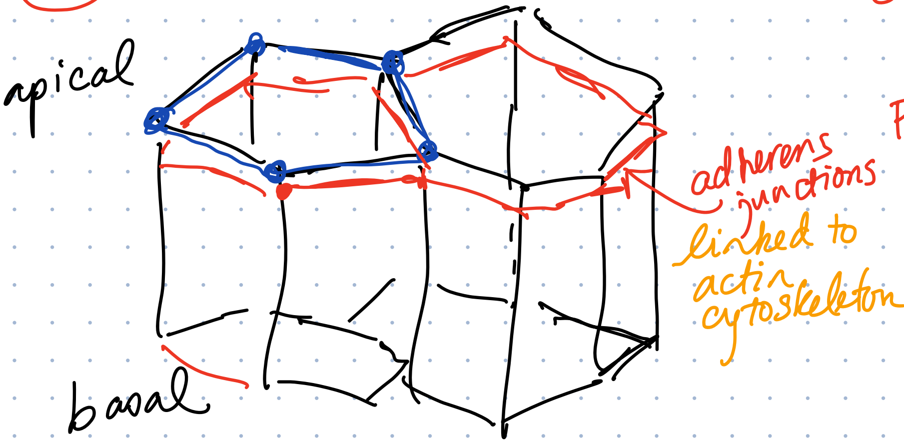
model parameter - (chosen by modeler or by organism (e.g. encoded in DNA))

configurational variable - depends on $X_{i\mu}$ and $g_{\alpha i}$

$$\mathcal{U} = \frac{1}{2}\sum_\alpha' \boxed{k_\alpha}\left(\boxed{l_\alpha} - \boxed{l_{0\alpha}}\right)^2$$

↳ Note: Next week, Andrea Liu will discuss these as "adaptive degrees of freedom" that biology can use to "learn".

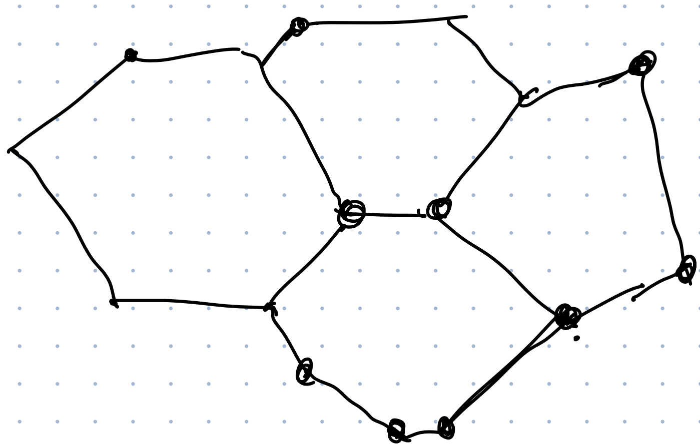
② Vertex models for biological tissues:



Nagai + Honda
Phil. Mag. B 2001
Farhadifar et al.
Current Biology 2007.
also
Hufnagel et al
PNAS 2007

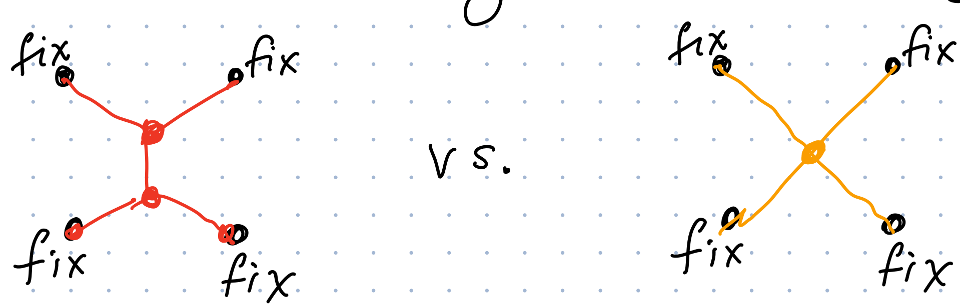
- monolayer of cells
- apical side looks like a network of polygons
  - positions of the vertices $\{x_{i\mu}\}$
  - incidence matrix $g_{\alpha i}$ (which edges connect which vertices)

⇓ gives rise to faces f with properties:
- cross-sectional area A_f
- cross-sectional perimeter P_f

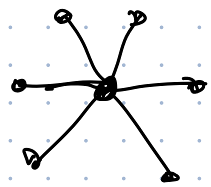


- in isotropic tissues, the vertices are usually 3-fold coordinated. Why?
  - Assume that each edge has the same tension σ (2d surface tension)
  - lowest energy $U = \sum_\alpha \sigma l_\alpha = \sigma \sum_\alpha l_\alpha$
  - minimizing $U \Rightarrow$ minimizing $\sum l$

Compare



- one can show (Exercise!) that the 3-fold coordinated system minimizes the energy (note, this breaks down in, e.g. anisotropic systems where σ's are different, can get "rosettes



- To proceed, we need to describe how a mechanical energy $\mathcal{U}$ arises from the vertices $\{x_{i\mu}\}$ and connectivity from $\{g_{\alpha i}\}$

model parameters

"adaptive DOF"

config. variable (depends on $x_{i\mu}$ + $g_{\alpha i}$)

$$\mathcal{U}_f = \frac{K_{Af}}{2}\left(\boxed{A_f} - A_{0f}\right)^2 + \sum_{\substack{\text{edges}\\ \text{in } f}} \frac{\Lambda_e}{2}\,\boxed{\ell_{edge}} + \frac{\Gamma_f}{2}\,\boxed{P_f}^2$$

Farhadifar

- cells are approximately incompressible. V=const
- in the monolayer, assume that there is a quadratic penalty for height fluctuations:
  $\mathcal{U} \sim (h-h_0)^2$
- $V = Ah$, so to linear order this generates a quadratic penalty on Area fluctuation

interfacial tension: generated by competition between adhesion + "cortical tension" – surface-tension like term generated by long-time behavior of actin-myosin cortex.

$\Rightarrow$ Farhadifar "contractile ring" of actin actively shrinks perimeter.

- could also be any other process that limits the perimeter of a cell, e.g. a limited pool of cadherins, see Latorre Nature 2018

Note: adhesion tends to elongate cell-cell interfaces in contact. But E-cadherin is orders of magnitude weaker than cortical tension. Probably more correct: E-cadherin regulates (often reduces) cortical surface tension at interfaces where it acts

Lecture 3:

- For a homogeneous system where all the model parameters are the same for every cell, this can be simplified:

$$\mathcal{U}_{tot} = \sum_f \mathcal{U}_f = \sum_f K_A (A_f - A_0)^2 + \underline{K_P (P_f - P_0)^2}$$

from $\Lambda \sum l_{edge} = \Lambda P$ and completing the square

$$P_0 = -\frac{\Lambda}{2\Gamma}, \quad \frac{\overline{K_A}}{2} = K_A \quad \frac{\Gamma}{2} = K_P$$

and finally we can nondimensionalize by $\underbrace{\sqrt{A_0}}_{\text{length}}$, $\underbrace{K_A A_0^2}_{\text{energy}}$

$$\boxed{\tilde{\mathcal{U}}_{tot} = \sum_f (a_f - 1)^2 + \tilde{K}_P (s_f - s_0)^2}$$

$$\underbrace{\tilde{K}_P = \frac{K_P}{K_A A_0}}_{\text{moduli ratio}} \;; \quad \underbrace{s_0 = \frac{P_0}{\sqrt{A_0}}}_{\text{"shape index"}}$$

there are two constraints on each face.

$$N_{faces} = \frac{(z-2)}{2} N_{vertices}$$

Constraint counting:

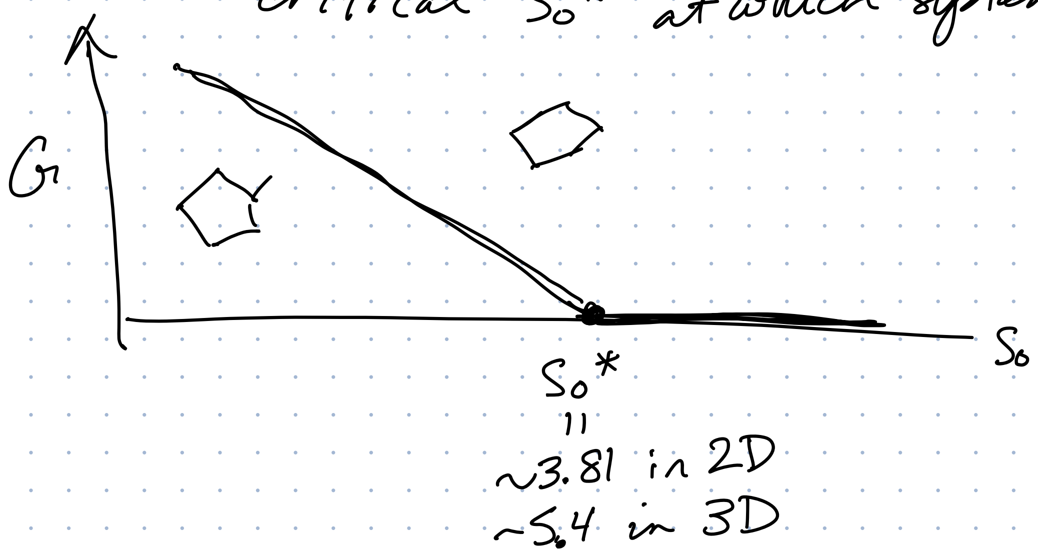
degrees of freedom: $\overset{2}{d}\, N_{vertices}$ — 2 for 2D vertex model

constraints: $M = 2 N_{faces} = (\overset{3}{z} - 2) N_{vertices}$

$$\underbrace{N_{vertices}}_{\text{constraints}} < \underbrace{2N_{vertices}}_{N_{DOF}} \Rightarrow \text{underconstraind}$$

But $\exists$ one state of self stress at the transition

Similar to the spring network there is a critical s_0^* at which system becomes rigid



$\Rightarrow$ slides for Lecture 3

- vertex model examples
- Universality + finite frequency
- programming materials