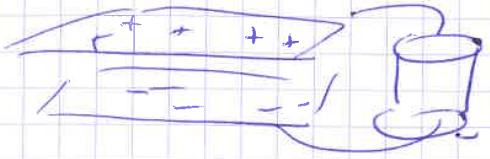
Stephanie

lecture 1

Lipid

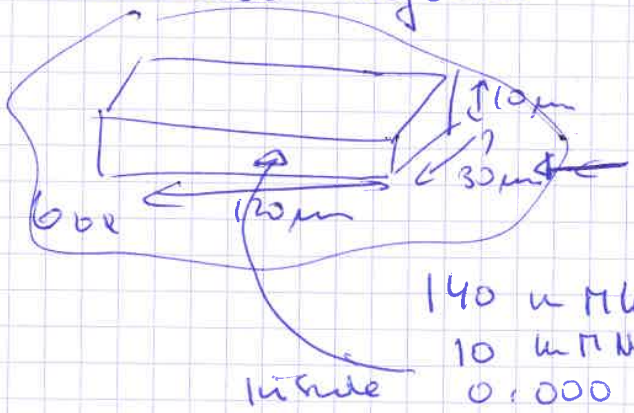
Membrane is like a capacitor



$I = C \frac{dV}{dt}$

Current $\frac{dV}{dt} = -I_{ion}$

Mammalian myocyte:



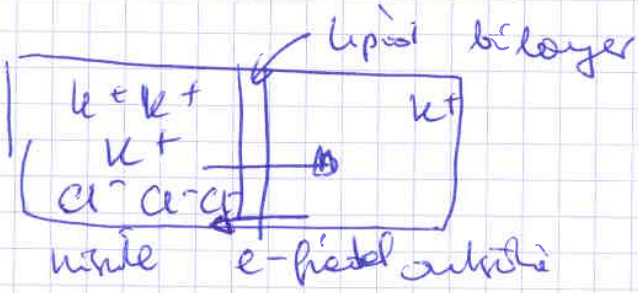
outside: 5 mM K^+, 140 μM Na^+, 2 mM Ca^{++}

inside: 140 mM K^+, 10 mM Na^+, 0.0001 mM Ca^{++}

Squid Giant Axon

400 mM K^+ 50 mM Na^+ 20 mM K^+ 491 mM Na^+

There are concentration cells.



if we have K^+ and Cl^- then the K^+ will diffuse but generate a charge.

$\mu = \mu_0 + RT \ln\{C\} + zFV$

$V_{inside} - V_{outside} = \frac{RT}{zF} \ln \frac{conc_{in}}{conc_{out}}$

Nernst potential — only the difference matters.

E

$E_{Na^+} = +55\ mV$

$E_{K^+} = -72\ mV$

If you are at $-72\ mV$ and you open a sodium channel. If Sodium goes in,

sodium spike.

opens a sodium channel.

What is the ATP consumption of one skype.

The Hodgkin Huxley model.

cellular

Memory capacitors / ~~capacitors~~ resistors.

ionic

The Fitzhugh Nagumo model

$$\frac{dV}{dt} = V + V^3 - W - I$$

$$\frac{dW}{dt} = 0.08\,(V + 0.7 - 0.8W)$$

Puzzle: 12 coins, 1 coin is counterfeit

you are given a balance — simple balance

You can weigh coins against each other.

which is counterfeit?

Is it heavy or light?

minimal number of weighings?

What would Obama do? he would run in the

Amutie

lecture 1

Evolution by under

human diversity:

genome $3 \cdot 10^9$ bp $\xrightarrow{2 \text{ chromo}}$ $6 \cdot 10^9$ bp

1 diff / 10^3 bp → 3×10^6 bp diff cell between chrom.

human mutation rate: $2 \cdot 10^{-8}$ / bp / generation.

etc → cancel exhale.

Leonid

lecture 1.

Chromatin Physics

Human / mouse	Single cell embryos	Bacteria
Genome $3 \cdot 10^9$ bp	$5 \cdot 10^7$ bp	$5 \cdot 10^6$ bp
Exome (2-4)		

G1: zygote ♀ + ♂ → homologs chr1 ♀ chr1 ♂

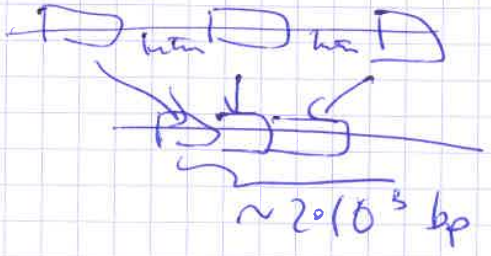
G2: zygote 2 sisters } 4 × sisters chr1 ♀ chr1 ♂ / chr1 ♀ chr1 ♂

S: replicate.

we all different in 1/1000 bp are different (~0.1%)

genes 25000

Exon1 Exon2 Exon3



~ $2 \cdot 10^3$ bp

Exons 60000 ~ 10^3 bp 3000

$25000 \cdot 2 \cdot 10^3 = 50 \cdot 10^6$

$\frac{50 \cdot 10^6}{3 \cdot 10^9} \sim 1.6 \cdot 10^{-3}$ (≈ 1.5%)

So this is still a horizontal part of the genome.

Duration time

~24 h

[~15 min]

M-phase

~1 h

(in early stages of dev. a couple of minutes)

Time

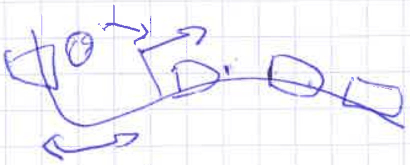
~1 h

~1 h

[~20 min]

regulating elements in yeast and bacteria

in humans they can bind far from the gene.



is it close in space?

it's very dependent.

500 bp

~10^3-10^6 bp.

humans have more TF per gene than bacteria

early metazoans start having enhancers.

In humans percent coding 1.5%.

in bacteria $\frac{3000 \text{ genes} \times 1000 \text{ bp}}{5 \cdot 10^6 \text{ bp}}$ ~ 60%.

Genome in 3D

length of genome in a cell: 1 bp = 0.3 nm

human	yeast	Bacteria
10^6 μm	6 mm	1.5 mm
	$6 \cdot 10^3$ μm	$1.5 \cdot 10^3$ μm

Rate of DNA synthesis $\simeq$ 0.2–1 kb/s

If there was 1 origin of replication it would take 10^6 sec.

So there are multiple origins.

$\# \sim 10^3$ origins.

$\rightarrow 5 \cdot 10^3$ sec! But only one origin.

$\Rightarrow$ one after the other. You don't want to finish . nested origin!

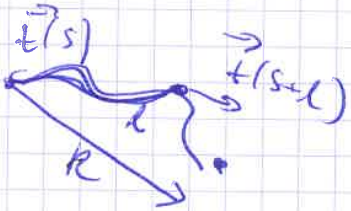
We do not know where the enzymes origin of replication.

Packing in the DNA.

Polymer physics

freely jointed chain

L - length of polymer.



$\langle \vec{t}(s)\, \vec{t}(s+L) \rangle \sim e^{-L/l_p}$ l_p - persistence length.

$\langle R^2(L) \rangle \sim 2L \cdot l_p = L \cdot B$

$\uparrow$ due to end distance.

- no excluded volume
- no topology.

$b = 2 l_p$ - Kuhn's length.

Random walk $\langle R^2 \rangle = N b^2$

So polymer behaves as a random walk with step of persistence length,

$R \sim N^{1/2}$ $\leftarrow$ This is universal, avoid excluded volume.

$R \sim N^{0.6}$ in 3D.

$l_p^{DNA} = 50\ nm = 150\ bp.$

$R(L) = 300\ \mu m.$

So it will not fit into a nucleus of 10 µm.

R(one dimension) ~ 30–60 µm. Poss[illegible] [illegible]

Yeast $R(L) \sim 20\ \mu m$
R(one dim) ~ 5 µm we have 3 µm.

bacteria 10–15 µm we have 1–2 µm.

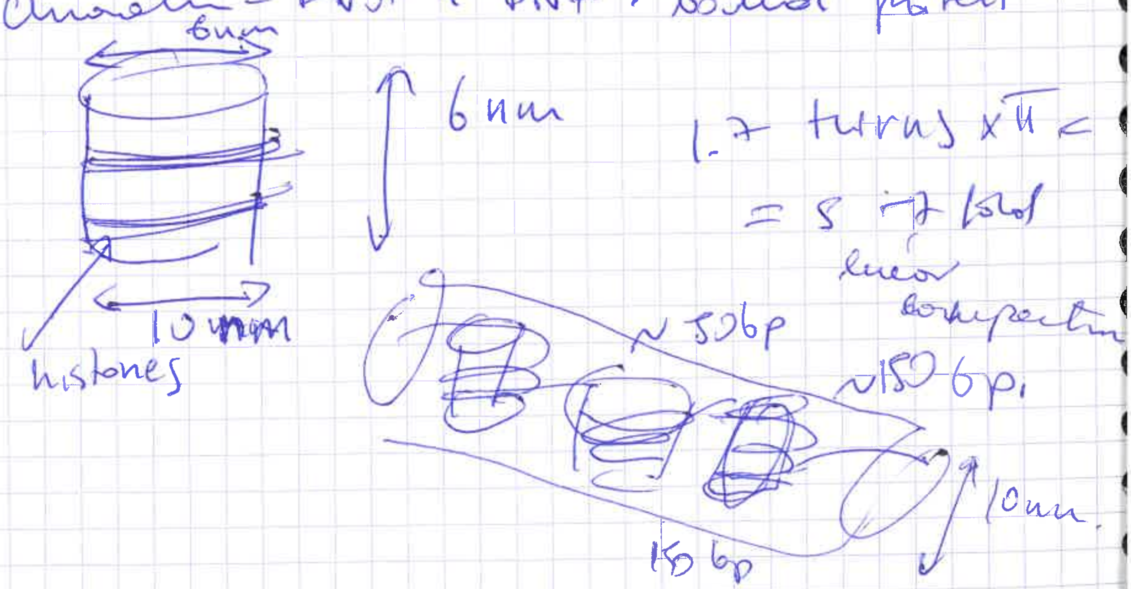
human: Volume fraction of DNA ~ 1%. 5%.
$V_{DNA} = 3 \cdot 10^{-6}\ \mu m \cdot 10^{6}\ \mu m = 3\ \mu m^3$
$V = 500\ \mu m^3$

yeast: 0,06%.
$3 \cdot 10^{-6}\ \mu m \cdot 6 \cdot 10^{3}\ \mu m = 20 \cdot 10^{-3} = 0,02\ \mu m^3$

~~bacteria~~ = 0,6%.

How does it fit.

Chromatin = DNA + DNA-bound protein

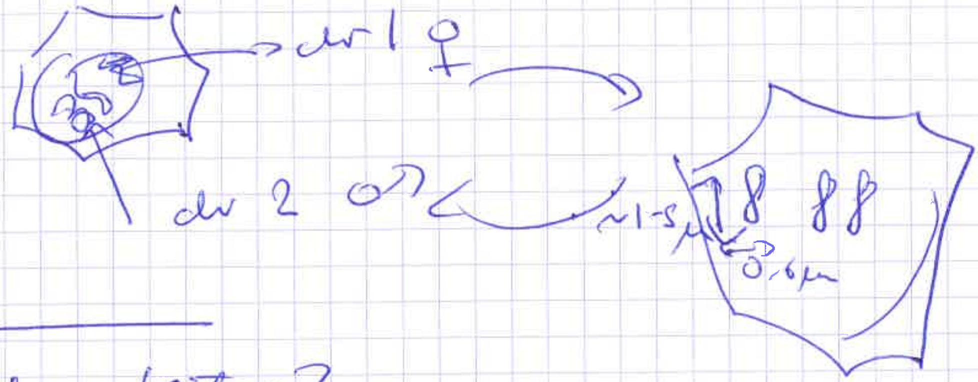


1.7 turns × π = 5 ... [illegible]

$l_p \sim$ 3-5 nucleotide = nm

[illegible] 10 nm fiber.

Interphase G_1-S-G_2



Armuta leitner?

selection. mutation gaussian noise

$$\frac{dx}{dt} = \Delta F_{ab}\, x(1-x) - \frac{\mu}{2}\left(x-\frac{1}{2}\right) + \chi_x(t)$$

$x = \frac{N_a}{N_a+N_b}$ sex ↑ ↑↑↑↑ . . ↓↓↓↓ household N_a N_b

$$\langle \chi_x(t)\rangle = 0$$

$$\langle \chi_x(t)\chi_x(t')\rangle = \frac{1}{N}x(1-x)\,\delta(t-t')$$

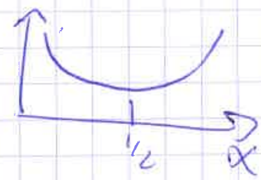
Probability density

$$\frac{dP(x,t)}{dt} = \left[\frac{1}{2N}\frac{\partial^2}{\partial x^2}x(1-x) - \frac{\partial}{\partial x}\Delta F_{ab}\,x(1-x) - \mu\frac{\partial}{\partial x}(1-2x)\right]P(x,t)$$

equilibrium (neutral).

$$P_{eq}(x) = \frac{1}{Z}\left[x(1-x)\right]^{-1+2\mu N}$$

$$\langle x\rangle = \frac{1}{2} \qquad \langle x(1-x)\rangle \simeq \mu N$$



D-dimensional evolution 30.5

$x_a + x_b + x_c = 1$ $N_a + N_b + N_c = 1$

$$\langle \chi_a(t)\chi_b(t')\rangle = \delta_{ab}\,\delta(t-t')$$

$$\chi_{x_a} = \sum_i \frac{\partial x_a}{\partial N_i}\chi_{N_i} \rightsquigarrow \langle \chi_{x_a}(t)\chi_{x_b}(t')\rangle = \begin{cases} x_\alpha(1-x_\alpha) & \alpha=\beta \\ -x_\alpha x_\beta & \alpha\neq\beta \end{cases}$$

$g(x)$

$$ds^2 = \sum g_{\alpha\beta}\,dx_\alpha\,dx_\beta$$

$$g^{\alpha\beta} \rightsquigarrow g_{\alpha\beta} = g^{\alpha\beta}$$

$$\frac{\partial P(x,t)}{\partial t} = \left[\frac{1}{2N} \frac{\partial^2}{\partial x_\alpha \partial x_\beta} g^{\alpha\beta}(x) + \frac{\partial}{\partial x_\alpha} g^{\alpha\beta}(s_\beta + m_\beta) \right] P(x,t)$$

$s_\beta = \frac{\partial}{\partial x_\beta} F$ — mutation field

$$m_\beta = \frac{\partial}{\partial x_\beta} M \qquad m = \frac{\mu(1-2x)}{x(1-x)}$$

Phenotype Stabilization

$$E = \sum E_i \sigma_i$$

$$\Gamma = \bar{E} = \sum_{\alpha \text{ types}} E_\alpha x^\alpha \sim \int E\, \omega(E)\, dE$$

$$\Delta = \int (E-\Gamma)^2 \omega(E)\, dE$$

$$f(E) = -c_0 (E - E^*)^2 \rightarrow F = \int f(E)\, \omega(E)\, dE = -c_0(\Gamma - E^*)^2 - c_0 \Delta$$

$$\frac{d\Gamma}{dt} = \frac{d}{dt} \int E\, \omega(E)\, dE = \int E\, (f(E) - F)\, \omega(E)\, dE$$

$$\frac{dx}{dt} = (f_a - F)\, x$$

$\rightarrow f_a x + f_b (1-x)$

$\Delta f_{ab}(1-x)$.

multiply it out:

$$\frac{d\Gamma}{dt} = \frac{d}{dt} \sum E_\alpha x^\alpha = \sum_\alpha E_\alpha \left(f(E_\alpha) - F \right) x^\alpha$$

$-c_\alpha (E_\alpha - E^*)^2 \qquad \rightarrow -c_0(\Gamma - E^*)^2 - c_0\Delta$

$$\frac{d\Gamma}{dt} = -c_0 \int E \left[(E-E^*)^2 - (\Gamma - E^*)^2 - \Delta \right] \omega(E)\, dE$$

$(E-\Gamma)^2 + (\Gamma - E^*)^2 - 2(E-\Gamma)(\Gamma - E^*)$

$$= \Delta \left[-2c_0 (\Gamma - E^*) \right]$$

Mutations:

$$\delta\Gamma = \frac{1}{N} \sum_{\alpha \text{ mutated}} E_i \sigma_i^\alpha$$

$\sigma = 1 \xrightarrow{\text{mutation}}_{1 \to 0} \delta\sigma = -1$

$0 \xrightarrow{0 \to 1} \delta\sigma = 1$

$\Big\}\ \delta\sigma = -2(\sigma - \tfrac{1}{2})$

$$\text{so } \delta\Gamma = \frac{1}{N}\sum \varepsilon_i' \left[-2\mu \left(\sigma_i^\alpha - 1/2 \right) \right] =$$

$$= -2\mu \left[\underbrace{\sum_{\substack{i \text{ protein} \\ \alpha \text{ solvent}}} \varepsilon_i \sigma_i^\alpha}_{\Gamma} - \frac{1}{2N} \sum_{i,\alpha} \varepsilon_i' \right]$$

$$= -2\mu \left(\Gamma - \frac{\sum \varepsilon_i'}{2} \right)$$

then redo for Holovitic pot.

$$\frac{d\Gamma}{dt} = \underbrace{-2\mu (\Gamma - \Gamma_0)}_{\text{mutation}} - \underbrace{2\Delta \frac{C}{E_0^2} (\Gamma - E^*)}_{\text{selection}} + \underbrace{\sqrt{\frac{\Delta}{N}}\, \chi_\Gamma}_{\text{Holovitic genetic drift}}$$

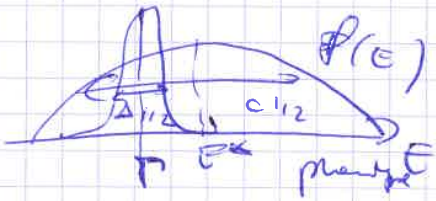
similar eqn for diversity, Δ,

$$f(E) = f^* - \frac{C}{E_0^2} (E - E^*)^2$$

→ solution Boltzmann type equilibrium solution

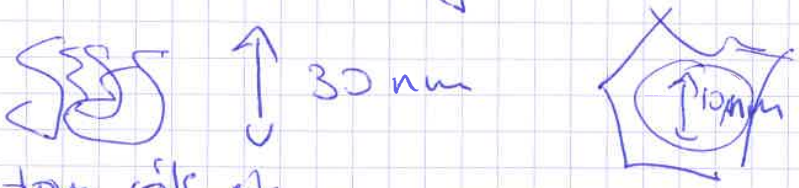
after separation of time scales $Q_{eq}(\Gamma) = \frac{1}{Z} Q_0(\Gamma)\, e^{2N F(\Gamma)}$

if you do not have separation of time scales then have a cloud so no equilibrium.



Genome in 3D

1. Human (mammalian genome).



random coil of freely joined chain

Hi-C - technique for linking how genomes fold. Incipit - microscopy how genome is folded in the cell.

In microscopy you can take two kind of photos and measure the spatial distance between them.

This is done on fixed cells, with a DAPI stain. Nothing moves in these cells,

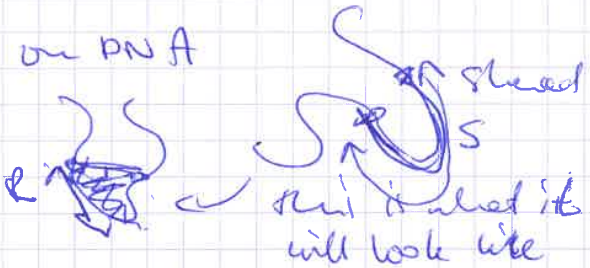
1. Multiplex . imaged(i,j) → result of this round $f_{ij}(R)$
2. DNA staining

← more distance.

you stain a whole region on DNA

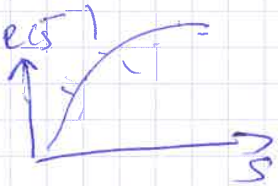
result of this method:

R(S)



3. Traditional techniques.

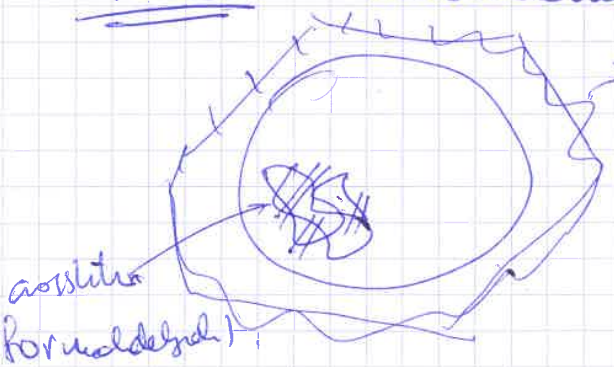
take two probes



← old techniques.

R_{ij} ← new techniques

Hi-C Chromosome conformation capture,



it is done for ~10^6 cells at a time (microscopy 1 cell).

Then chop DNA into pieces using a restriction enzyme.

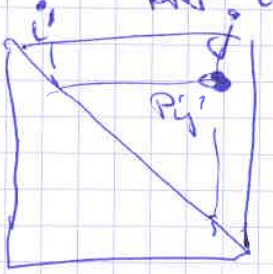
as a result (you keep only the segment inside a nucleus). You get bits of DNA that are ligated.

So you get one piece of DNA of 6Mb that where for, apart on the chromosome,

Then sequence.

and map,

scales of 100 bp



maps of contact frequency

Aside: how many bp to uniquely identify a place on the human genome? $\log_4 N_{bp}$,

$R_c \sim 100$ nm ← distance between cross linked bp,

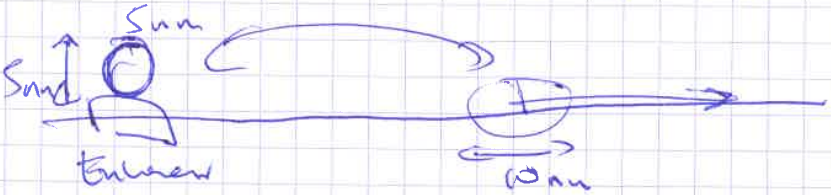
$R_c \sim 40$ nm in μC (new technique)

It depends on the diversity of the process,

most of the data are in the ~~mitochondrial~~ interphase (95%) and 5% in metaphase.

You can try and synchronize.

Active regions (gene rich) are in the middle of the nucleus in humans and mammals and gene poor are at the periphery

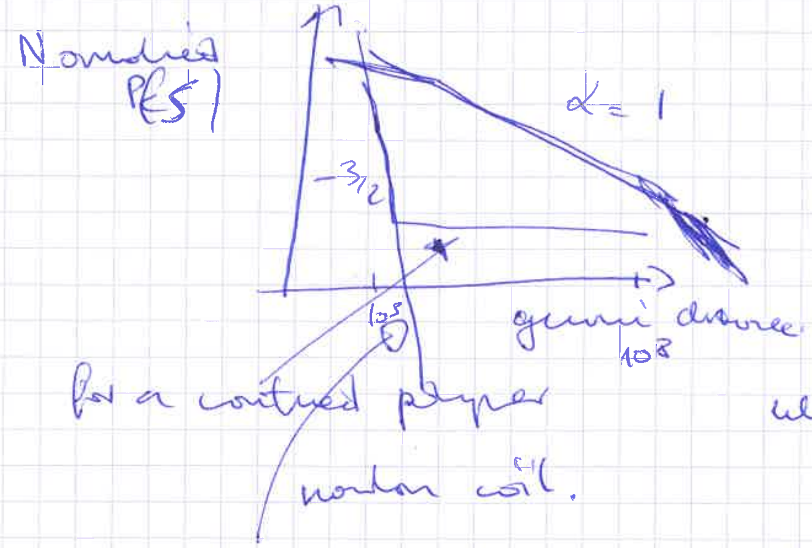


so they have to come within 5nm

but the resolution is R~40nm for Hi-C.

and 40nm for μC → so it mainly picks up structural information and not functional.

It's like trying to see who talks to whom ~~talking~~ by imaging a smile radius.



$P(s) \sim s^{-\alpha}$
anomaly reproducing
between vertebrates

open question:
what kind of organization
gives you this scaling?

$P(\ldots)_{ij}$ from models → $P(s = |i-j|)_{i,j}$

RW ← random walk

Predictions for uncrossing $R(s) \sim s^{1/2}$

compact state $R(s) \propto s^{1/3}$

Stephanie
lecture 2

Information in single spikes

1D stimulus

$r(t) \Leftarrow \langle \rho(t) \rangle = \sum \delta(t - t_i)$

Swap the trial average for a time average. → ergodic assumption

$I[m(t), r(t)] = S(M) - S(M|R)$

ensemble of m & ensemble of r.

$$S(M|R) = \sum_{r_i} P(r_i)\left[-\sum_{m_i} P(m_i|r_i)\log_2 P(m_i|r_i)\right]$$

$$P(m|r) = \frac{P(r|m)P(m)}{P(r)}$$

$$I(M,R) = -\sum_{m_i} p(m_i)\log p(m_i) + \sum_{r} p(r=1)\left[\frac{p(r=1|m_i)p(m_i)}{p(r=1)}\times\right.$$

$$\left.\times\log\frac{p(r=1|m_i)p(m_i)}{p(r=1)}\right] + \sum_{m_i} p(r=0)\left[\frac{p(r=0|m_i)p(m_i)}{p(r=0)}\times\right.$$

$$\left.\log(\ldots)\right]$$

Make bins such that Δt is such that either $r=0$ or $r=1$.

① $P(r=0) = 1 - P(r=1)$

Swap Shannon average for true average.

② $\sum_{m_i} P(m_i) f(m_i) = \frac{1}{N_t}\sum_t f(t)$

$$= -\sum_m p(m)\log(m)\left[1 - p(r=1|m) - (1-p(r=1|m))\right] +$$

$$+\sum_m p(m)\left[p(r=1|m)\log\frac{p(r=1|m)}{p(r=1)} +\right.$$

$$\left.+(1-p(r=1|m))\log\frac{1-p(r=1|m)}{1-p(r=1)}\right]$$

② $p(r=1|m=m(t_i)) = R(t_i)\Delta t \qquad \bar{R} = \langle R(t)\rangle_t$

$$I(M,R) = \frac{1}{N_t}\sum_{t_i}\left[R(t_i)\Delta t\log\frac{R(t_i)}{\bar{R}} +\right.$$

$$\left.+(1-R(t_i)\Delta t)\log\left[\frac{1-R(t_i)\Delta t}{1-\bar{R}\Delta t}\right]\right]$$

take $\Delta t \to 0$ which makes us lose the 2nd term

$$I(M,R) \simeq \frac{1}{N_t}\sum_{t_i} R(t_i)\Delta t\log_2\left(\frac{R(t_i)}{\bar{R}}\right)$$

$R(t_i)$ ← response when there is a Muller

$\bar{R}$ ← average response.

$$\left[\frac{\text{bits}}{\text{spike}}\right]\frac{I(M,R)}{\bar{R}\Delta t} = \frac{1}{T}\sum_{t_i}\frac{R(t_i)}{\bar{R}}\Delta t\log\frac{R(t_i)}{\bar{R}}$$

continuous limit

$$I(\text{single spike, S}) = \frac{1}{T}\int_0^T dt\,\frac{r(t)}{\bar{r}}\log_2\frac{r(t)}{\bar{r}}$$

But different stimuli will give different numbers of I of 1 spike.
It encodes the frequency of spikes but not their ordering.
It makes an assumption that the spikes are not correlated.

Stephanie lecture 3

Gaussian channel.
$r = f(m) = \Phi(m) + z$ ~ Gaussian $\in (0, \sigma^2)$

maximize $I(R,M)$?

$I(R,M) = S(R) - S(R|M)$ — entropy of mixture of S,

$= S(R) - \langle S(z|m) \rangle_m$ — for a particular message this is just a number.

For discrete variables the uniform distribution has the maximum entropy

$p(R,M) = p(R|M)p(M)$ — $p(z)$

$I(R,M) = S(R) - S(z)$ — this is constant

$S(R) = -\sum_i p(r_i) \log p(r_i)$ $\quad \sum_i p(r_i) = 1$

$\mathcal{L} = S(R) - \lambda\left[1 - \sum_i p(r_i)\right]$

$\frac{\delta \mathcal{L}}{\delta p(r_i)} = \frac{\partial \mathcal{L}}{\partial p(r_i)} = -\frac{p(r_i)}{p(r_i)} - \log\left(p(r_i)\right) + \lambda = 0$

$p(r_i) = e^{-1+\lambda}$

$e^{-1+\lambda} = \frac{1}{N}$

$p(r_i) = \frac{1}{\text{Number}}$

Gaussian channel:

$r = \phi(m) + z$

more info $p(r) = \frac{1}{N}$ $\quad p(r) \leq \frac{\Delta r}{r_{max}}$ $\quad N = \frac{r_{max}}{\Delta r}$

$p(m)$ fixed

what should $\Phi(m)$ be to maximize $I(R,M)$?

$p(m)\,\Delta m = \underbrace{p(r)\Delta r}_{\text{prob density}}$.

$p(m)\,\Delta m = p(r)\,[\Phi(m+\Delta m) - \Phi(m)]$

to maximize $p(r)/\Delta r = \left(\frac{\Delta r}{r_{max}}\right)\frac{1}{\Delta r}$

$p(m)\,\Delta m = \frac{1}{r_{max}}\left[\Phi(m+\Delta m) - \Phi(m)\right]$

assume $\Phi(m)$ is monotonic in m

$r_{max}\,p(m) = \left(\frac{\Phi(m+\Delta m) - \Phi(m)}{\Delta m}\right)$

$\int_{m_{min}}^{m} dm' \frac{d\Phi(m')}{dm'} = \int_{m_{min}}^{m} r_{max}\,p(m')\,dm'$

$\Phi(m) = r_{max}\int_{m_{min}}^{m} p(m')\,dm'$.

Old school way $I(m,R) = S(R) - S(R|m)$

Another lecture:

$g^{\alpha} = \begin{cases} x^{\alpha}(1-x^{\alpha}) & \text{if } x_{\alpha} = x_{\beta} \\ -x^{\alpha}x^{\beta} & x_{\alpha} \neq x_{\beta} \end{cases}$

$g^{rr} = \sum_{\alpha\beta} \frac{\partial r}{\partial x^{\alpha}} \frac{\partial r}{\partial x^{\beta}} g^{\alpha\beta} = \sum_{\alpha\beta} E_{\alpha}E_{\beta}\,g^{\alpha\beta} =$

$= \sum E_{\alpha}E_{\beta}\left(\delta^{\beta}_{\alpha}\,x^{\alpha}(1-x^{\alpha}) - (1-\delta_{\alpha}^{\beta})\,x^{\alpha}x^{\beta}\right)$

$= \Delta$

$g^{rr} = \Delta$

$g^{r\Delta} = \mu_3 \simeq 0$

$g^{\Delta\Delta} = \mu_4 - \Delta^2 = 3\Delta^2 - \Delta^2 = 2\Delta^2$

Relation: $S_\Delta = -4\mu(\Delta - E_0^2) - \left(\frac{\Delta}{N}\right)$ ⇝ Bts calculer

$\Delta = \overline{E^2} - \Lambda^2$

calculer $\frac{d}{dt} S\Delta = \rho^{\Delta\Delta} \frac{\partial F}{\partial \Delta} + \rho^{\Delta\Lambda} \frac{\partial F}{\partial \Lambda} = -2C_0\Delta^2$

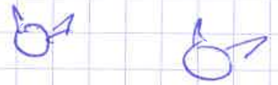
$F = -C_0(T - E^*)^2 - C_0\Delta$

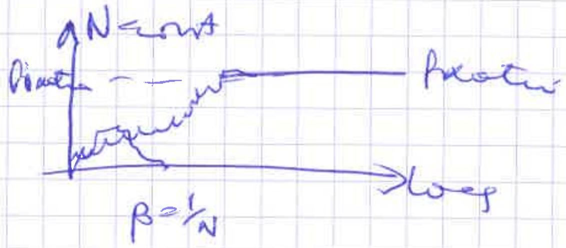
$$\frac{dQ}{dt}(\Lambda, \Delta, t) = \left[\frac{1}{2N}\frac{\partial^2 \Delta}{\partial \Lambda^2} + \frac{1}{2N}\frac{\partial^2}{\partial \Delta^2}(-2\Delta^2) + \frac{\partial}{\partial \Lambda} 2\mu(\Lambda - \Lambda_0)\right.$$
$$+ \frac{\partial}{\partial \Delta}\left[4\mu(\Delta - E_0^2) + \frac{\Delta}{N}\right) + \frac{\partial}{\partial \Lambda} 2C_0\Delta(\Lambda - E^*)$$
$$\left. + \frac{\partial}{\partial \Delta} 2C_0\Delta^2\right] Q(\Lambda, \Delta, t).$$

Leonid

Lecture 4 Cancer evolution.

Population genetics.

1. 



2. Prob of fixation

for neutral mutation $\pi(s=0, p_0) = p_0$

3. Selection: $s>0$ $s \ll 1$

p_0 $1-p_0$

$1+s$ 1

$$\pi(s, p_0) = \frac{1-e^{-2Nsp_0}}{1-e^{-2Ns}}$$

$p_0 = 1/N$

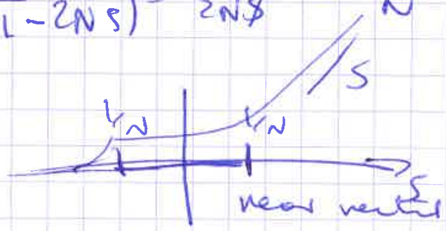
$$= \frac{1-e^{-2s}}{1-e^{-2Ns}}$$

$Ns \ll 1$

$$\pi(s) = \frac{2s}{1-(1-2Ns)} = \frac{2s}{2Ns} = \frac{1}{N}$$

$Ns \gg 1$ $s \gg 1/N$

$\pi(s) \simeq 2s$



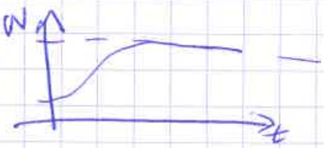
humans $N_{eff} = 10^3 - 10^4$

mouse $N = 10^5 - 10^6$

mutations Goode & Getz Keen 412 Science 2009.
in healthy cells.

Cancer evolution (with drivers and passengers) 1840

$N \neq$ const ① $\frac{dN}{dt} = N\left(1 - \frac{N}{K}\right)$ K carrying capacity



② Add mutations

$$\frac{dN}{dt} = N\left(1 - \frac{N}{K}\right)$$

(B) birth rate, death (D) $D = \frac{N}{K}$ will depend on mutations

$$B = \frac{(1+s_d)}{(1+s_p)^{n_p}} \qquad D = \frac{N}{a}$$

n_d – # of driver mutations non-epistatic model
s_d – selection coefficient of drivers
s_p – selection coefficient for passengers.
n_p – # of passengers.

separate heads and tails cloth

$$\frac{N(n_d+1)}{N(n_d)} = \frac{(1+s_d)^{n_d+1}}{(1+s_p)^{n_p}}$$

difference of one term

$$\frac{N(n_d)}{N(n_d)} = \frac{(1+s_d)^{n_d}}{(1+s_p)^{n_p}}$$

$$\Delta N = N(n_d+1) - N(n_d) = s_d N(n_d)$$

$$\Delta N = N(n_p+1) - N(n_p) = -s_p N(n_p)$$

(3) Mutations

passenger driver passenger driver

μ – mutation rate per bp per cell divi — target size (bp)

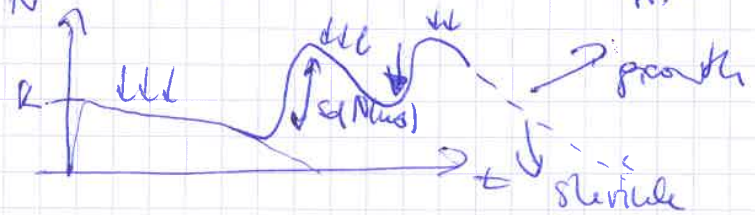
T_d — more passengers $T_p \gg T_d$

$(s_p > 0)$ T_p — but effect of drivers if large $s_p \ll s_d \ll 1$

consider only non-neutral passengers.

passengers emit at rate $T_p n_p \mu$

N drivers emit at rate $T_d n_d \mu$.



Velocity of growth: $V = v_d - v_p$

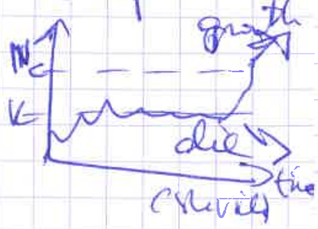
$V_d = \underbrace{T_d \cdot \mu \cdot N}_{\text{prob. of getting driver}} S_d \cdot \underbrace{S_d \cdot N}_{\Delta N} = T_d \mu N^2 S_d^2$

prob. of fixating drivers.

$V_p = T_p \mu N \; {}^{1}/_{N} \cdot S_p \cdot N = T_p \mu N S_p$.

N_c : $V_d = V_p$ $\quad T_d \mu N_c^2 S_d^2 = T_p \mu N_c \cdot S_p$

$$N_c = \frac{T_p}{T_d} \frac{S_p}{S_d^2}$$



small cancer lesions should reduce themselves

There is also a critical mutation rate, $\mu_c \sim S_d$

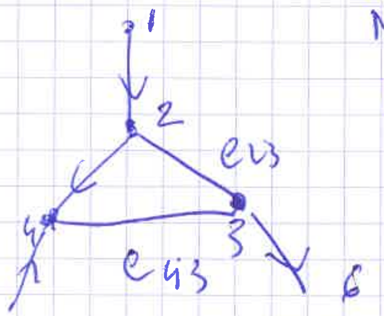
above μ_c a driver would be getting so many mutations (passengers) that it cannot support them so that it goes down.

more passenger mutations increase the lifetime => cancer grows more slowly.

Orit Peleg

Bee swarms. Bees need to adapt to different shapes,

Eleni' lecture 1



N nodes V

M links E oriented

$e_{ij} \in E$

$e_{ij} = \{u_i, u_j\}$

incidence matrix $\Rightarrow N \times M$

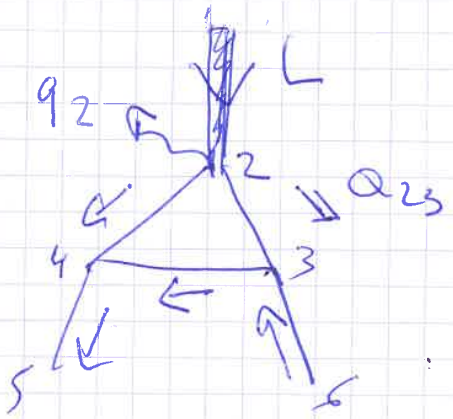
$e_1 = \{1,2\}$
$e_2 = \{2,3\}$
$e_3 = \{2,4\}$
$e_4 = \{4,3\}$
$e_5 = \{5,4\}$
$e_6 = \{3,6\}$

outgoing node 1 $\quad \Delta^T$

$\Delta = $ (edge e_1 ... ; node 1, 2, ... ; incoming node 2)
$$\begin{bmatrix} -1 & 0 & \\ 1 & -1 & -1 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

$\leftarrow$ no interaction with them.

$\sum_i \hat{\Delta}_{ij} = 0$



Flow field Q_{ij}

I have to choose what is my positive orientation.

$Q \in N \times N$ antisymmetric

$\sum_k Q_{ki} = 0$ mass conservation.

If the node is a leaky node:

$\sum_k Q_{ki} = q_i$ net current.

$$\boxed{\Delta^T \vec{Q} = \vec{q}}$$ conservation.

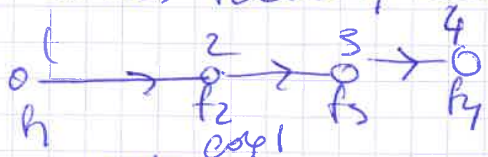
$$\vec{Q} = \begin{bmatrix} Q_{12} \\ Q_{23} \\ Q_{24} \\ Q_{43} \\ Q_{50} \\ Q_{63} \end{bmatrix}$$ $M \times 1$ ← selected based on the paper.

Fundamental theorem of calculus.

$$\int_a^b f(t)\,dt = F(b) - F(a) \quad \text{where } \frac{dF}{dt} = f$$

$$\int_{\Omega} d\tilde{\omega} = \int_{\partial\Omega} \tilde{\omega}$$ integral over the boundary.

The point of this is to introduce the equivalent of Stoke's theorem, Gauss' theorem etc on graphs.



$$\Delta^T = \begin{bmatrix} -1 & 0 & 0 \\ 1 & -1 & 0 \\ 0 & 1 & -1 \\ 0 & 0 & 1 \end{bmatrix}$$ (each column = edge; each row = node)

take transpose and act on $\begin{bmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \end{bmatrix}$

$$\Delta^T \vec{f} = \begin{bmatrix} f_2 - f_1 \\ f_3 - f_2 \\ f_4 - f_3 \end{bmatrix}$$

$$d \to \nabla = \begin{bmatrix} 1 \\ 1 \\ 1 \end{bmatrix}$$

$$\langle \Delta f_{12}, \vec{\nabla} \rangle = f_4 - f_1$$

$$\hat{\Delta}^T \cdot \vec{\tau} = \begin{bmatrix} -1 \\ 0 \\ 0 \\ 1 \end{bmatrix}$$

$$\langle f , \hat{\Delta}^T \vec{\tau} \rangle = f_4 - f_1$$

$$\boxed{\langle \hat{\Delta} \vec{f} , \vec{\tau} \rangle = \langle \vec{f} , \hat{\Delta}^T \vec{\tau} \rangle}$$

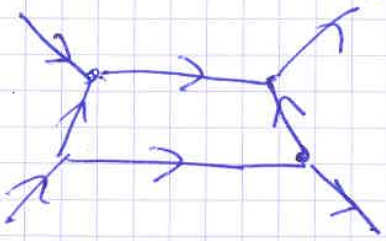
If I call f = pressure p then I get pressure difference

$$\langle \hat{\Delta} \vec{p} , \vec{\tau} \rangle = \langle \vec{p} , \hat{\Delta}^T \vec{\tau} \rangle = p_4 - p_1$$

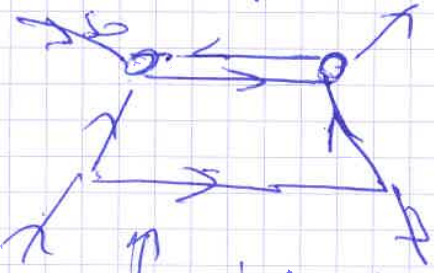
all the pressure drops along the edges.

the same as getting the pressure at the end vertex and subtract the left vertex. (so called pressure drop.

And this works for any graph.



that has flow in one direction on each edge



But any graph we will consider as in flow network.

So this is not allowed

$$Q_{ij} = (p_i - p_j) C_{ij}$$ ← conductance

↑ the flow that goes from i to j

is proportional to the pressure drops between these edges.

The larger the conductance C_{ij} the more flow you can have for the same pressure drop. The smaller C_{ij} the less flow for the same pressure drop.

$$\text{diag}(C)_{M\times M} = \begin{bmatrix} c_{12}c_{23}c_{24}c_{45}c_{56} & & 0 \\ & \ddots & \\ 0 & & c_{56} \end{bmatrix}$$

$$\vec{Q} = \text{diag}(C)\,\hat{\Delta}\,\vec{p}$$

Where does c_{ij} come from

You could have a more complicated relation $c_{ij} = f(\Delta p)$ and Taylor expand and keep the linear term.

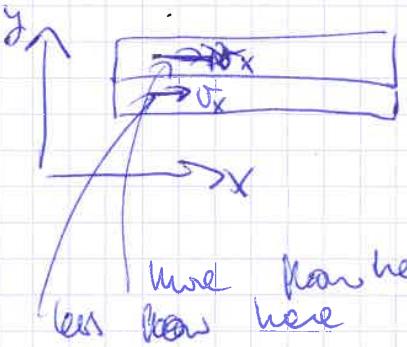
$$\hat{\Delta}^T = \begin{pmatrix} -1 & 0 & 0 \\ 1 & -1 & 0 \\ 0 & 1 & +1 \\ 0 & 0 & -1 \end{pmatrix} \qquad \hat{\Delta}\cdot\vec{p} = \begin{bmatrix} p_2 - p_1 \\ p_3 - p_2 \\ p_3 - p_4 \end{bmatrix}$$

$$\langle \hat{\Delta}\vec{f}, \vec{c} \rangle = 2f_3 - f_1 - f_4$$

$$\hat{\Delta}^T\vec{c} = \begin{pmatrix} -1 \\ 0 \\ 2 \\ -1 \end{pmatrix}$$

but this still holds. $\langle \vec{f}\,|\hat{\Delta}^T|\,\vec{c}\,\rangle = \langle \Delta f, \vec{c} \rangle$

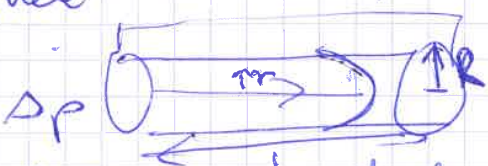
Poiseuille flow



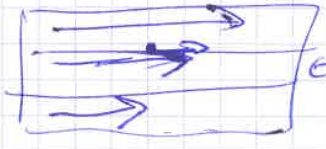
there is friction between these layers.

$$F = -\mu A \frac{dv_x}{dy}$$

pressure difference.



how much flow you get for this Δp.



this layer is dragged by the layer on the top and pulled back by the layer on the bottom.

You want to calculate the forces and because you are in a cylinder the area changes.

$$\Delta p \simeq -\mu L \frac{1}{r}\left(r \frac{dv}{dr}\right)$$

$$v \sim R^2 - r^2$$

$$Q \simeq \int_0^R v(r)\, 2\pi r\, dr$$

$$Q = \left(\frac{\pi R^4}{8 L \mu}\right) \Delta p$$

↳ Conductance.

This is super important for our basis.

Use (lecture 1)

Bio mimetic & active matter.

Many biological systems involve interactions between large #s of objects at high densities that are active — energy is injected at the smaller scales.

- condensed matter: predict emergent collective behavior
  - for fun equilibrium
  - what is the right level of model (not atoms or molecules).
  - different types of interactions / boundaries
    - alignment / polarity
    - steric / pressure / jamming or MIPS epithelium (motile polar rigid)

"active"

- local for each agent
  → not driven by a boundary condition or global bath.

Examples of active matter in biology,

Examples of active matter in biology.

(A) Definitions of active matter } lecture

(B) Statistical physics of single, non interacting particles)

i) Brownian

ii) self-propelled particles.

(C) Interactions + emergent behaviour } lecture 4.

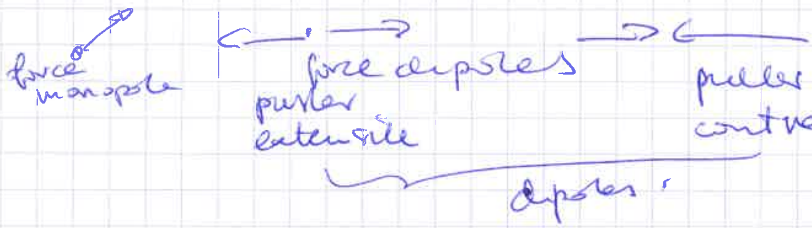
i) alignment + flocking

ii) steric interactions (metric-based) lecture 4(ii)

iii) shape-based interaction (topological) lecture 4

Classification of active matter:

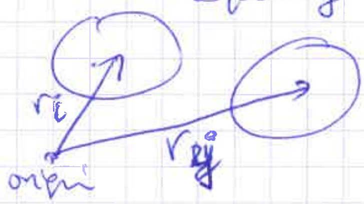
- type of force generation



Types of particle-particle interactions.

squishy objects

+ steric



metric $|r_i - r_j|$

another way to think about — OR —

if you think the interactions may be space filling → construct the Wigner-Seitz cell. or Voronoi tessellation

→ topological or neighbour based

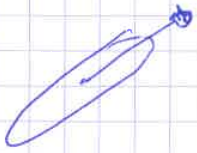
If I expand this → the relations looks the same.

+ alignment interactions

if each of my objects has an orientation associated with it.

} metric or topological rule.

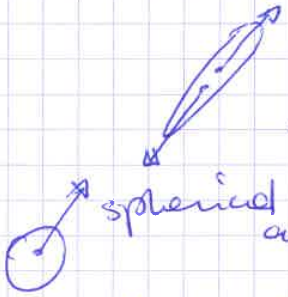
+ mixture of the above



polar objects that have a mixture of both, (eg. bacteria, fish, some cells)

they will align

and others have an elongated shape but they have no axis which way they will go



this is like liquid crystals test to change shape.

Types of interactions with the environment

↳ hydrodynamic interaction (walls, other particles) (not in this course)

→ drag (friction forces with substrate or other particles.

Interactions with global field: gravity, morphogen gradient.

B.) Non-interacting particles.

colloid in a solvent (Perrin)

$ma = \Sigma F$ ← effect of collisions.

$m\dot{v} = F_{pot} + F_{drag} + F_{random}$

$-\nabla U \quad -\zeta v \quad +\eta(t)$

McQuarrie → ref. for demystified.

for a spherical particle in 3D $\zeta = 6\pi\eta a$ ← particle radius

Characteristic timescale $\tau_m = m/\xi$

$$\langle |v(t)|^2 \rangle = \frac{d\Delta}{m\xi}\left(1 - e^{-2|t|/\tau_m}\right)$$

↑ autocorrelation timescale memory.

$t >> \tau_m \Rightarrow \Delta = \xi T$

$$\langle \Delta r^2(t) \rangle = \begin{cases} \frac{dT t^2}{5\tau_m} & t << \tau_m \text{ ballistic.} \\ & \text{(scales as } t^2\text{)} \\ \frac{2dT}{\xi}|t| & t >> \tau_m \text{ diffusive} \\ & \text{scales as } |t| \end{cases}$$

Contrast all of this to self-propelled particles.

$\Sigma F = ma$

You can go to the overdamped limit $\Sigma F = m\dot{v} \to 0$

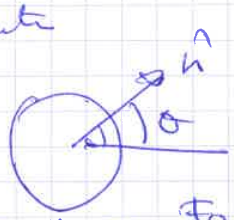
to a non-inertial system, neglect an inertial term.

$F_{drag} + F_{spp} + F_{interaction} = 0$

↑ this will be self propelled force

a force in a certain direction

$-\xi v + F_0 \hat{n} = 0$



So there is the idea that there is a preferred direction of motion $v_0 = \frac{F_0}{\xi}$

How does this apply for a self-propelled motion

$$\frac{d\vec{r}}{dt} = v_0 \hat{n}$$

$$\frac{\partial \theta}{\partial t} = \eta^R(t) \qquad \langle \eta^R(t)\, \eta^R(t') \rangle = 2D_R \delta(t - t')$$

Mean first displacement.

$$\frac{\partial x}{\partial t} = v_0 \cos\theta(t)$$

$$\frac{\partial y}{\partial t} = v_0 \sin\theta(t)$$

Ask about this average of velocity in the x direction

we know $\theta(t) = \int^t \eta^R(t')\,dt'$ (just the previous good old definition of η^R)

I want to use cumulants so I need cos → exp.

$$\cos\theta = \tfrac{1}{2}\left(e^{i\theta} + e^{-i\theta}\right)$$

$$\chi = \frac{v_0^2}{4}\left\langle \left[e^{i\theta(t)} + e^{-i\theta(t)}\right]\left[e^{i\theta(t')} + e^{-i\theta(t')}\right]\right\rangle =$$

$$\phi(t) = \theta(t) + \theta(t')$$

$$\omega(t) = \theta(t) - \theta(t')$$

because it's Gaussian: $\langle e^{i\theta}\rangle = e^{-\frac{\langle\theta^2\rangle}{2}}$

$$= \frac{v_0^2}{2}\left\langle e^{i\phi} + e^{i\omega}\right\rangle =$$

$$= \frac{v_0^2}{2}\left[e^{-\frac{\langle\phi^2\rangle}{2}} + e^{-\frac{\langle\omega^2\rangle}{2}}\right]$$

So now we can calculate $\langle\phi\rangle$ and $\langle\omega\rangle$

$$\langle\phi^2\rangle = \langle\theta^2(t) + 2\theta(t)\theta(t') + \theta^2(t')\rangle$$

$$\langle\theta(t)\theta(t')\rangle = \int^t\int^{t'}\langle\eta^2(\tilde t)\eta^2(\tilde t')\rangle\,d\tilde t\,d\tilde t' = 2D\int^t\int^{t'}\delta(\tilde t - \tilde t')\,d\tilde t\,d\tilde t' =$$

if $t' > t$:

$$\begin{cases} 2D\int^t 1\,d\tilde t = 2Dt \\ 2D\int^t 1\,d\tilde t' = 2Dt' \end{cases} = 2D\min(t,t')$$

$$\langle\omega^2\rangle = 2Dt + 2Dt' - 4D\min(t,t')$$

for $t < t'$: $\chi = \frac{v_0^2}{2}\left(e^{-1/2(2Dt + 2Dt' + 4Dt')} + e^{-1/2(2Dt + 2Dt' - 4Dt')}\right] =$

$$= \frac{v_0^2}{2}\left[e^{-6Dt - 2Dt'} + e^{-2D(t'-t)}\right]$$ → go over in steady state

for $t > t'$ $= \frac{v_0^2}{2}\left[e^{-2Dt - 4Dt'} + e^{-2D(t-t')}\right]$

in steady state

$$\langle v_0\cos\theta(t')\, v_0\cos\theta(t)\rangle = \frac{v_0^2}{2}e^{2D|t-t'|} \quad \left(\tau \sim \frac{1}{D}\right)$$

Now denote the RMS of self-propelled particles,

$\frac{dx}{dt} = v_0\cos\theta(t) \Rightarrow \langle x(t)^2\rangle = \int^t\int^{t'} A(\tilde t, \tilde t')\,d\tilde t\,d\tilde t'$

$$\langle x(t)^2 \rangle = \frac{v_0^2}{D}\left[\frac{t}{D} + \frac{1}{D}\left(e^{-Dt} - 1\right)\right]$$

each direction just adds up

for 3D dimensional system (above is 1D).

$$\langle (r(t))^2 \rangle = \frac{dv_0^2}{D}\left[\frac{t}{D} + \frac{1}{D}\left(e^{-Dt} - 1\right)\right]$$

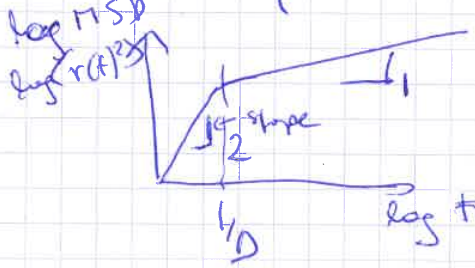
(d = dimension)

Mean squared displacement of SPP (self-propelled particle) → but just with rotational noise

Translational noise adds to that,

Take two limits of this eqn

$$\begin{cases} t << \frac{1}{D} & \langle r(t)^2 \rangle = \frac{dv_0^2 t^2}{2} \\ t >> \frac{1}{D} & \langle r(t)^2 \rangle = \frac{dv_0^2 t}{D} \end{cases}$$



a self propelled particle looks like a Brownian particle but for a very different reason and the cross-over time is different.

to detail $\langle \eta^R(t)\eta^R(t+t) \rangle = 2D_R\,\delta(t+t)$

The dimensionless number that describes this competition that describes this competition between self propelled SP speed and rotational noise is the

Peclet number $Pe = \frac{v_0}{2\pi D_R}$ ← rotational diffusion

↑ radius of particle.

You can also extract it for the orientation

Just in an experiment.

Say you have a trajectory

correlation of the orientational angle.

$$Pe = \frac{v_0}{2R D_R} = \frac{L}{2R} \Rightarrow L = \frac{v_0}{D_R}$$

why is $\frac{d\theta}{dt} = \eta^{R}(t)$

$\theta(t+\Delta t) = (\theta(t) + \eta)\,\Delta t$

how does the orientation change for normal step.

$Pe \ll \frac{2v_0}{R} \rightarrow$ Brownian

$Pe \gg \frac{2v_0}{R} \rightarrow$ you go in a straight line

Aguere

lecture 1

life at low Reynolds numbers

$$\partial_t \bar{u} + \bar{u}\cdot\bar{\nabla}\bar{u} = \nu\nabla^2 u - \frac{1}{\rho}\bar{\nabla} p + f$$

$\frac{u^2}{L}$ inertia $\frac{\nu u}{L^2}$ viscosity

$$\frac{\text{inertia}}{\text{viscosity}} = \frac{u^2/L}{\nu u/L^2} = \frac{uL}{\nu} = Re \quad [\text{Reynolds number}]$$

$Re \sim 10^{-5}$

$u \sim 20 \frac{\mu m}{s}$

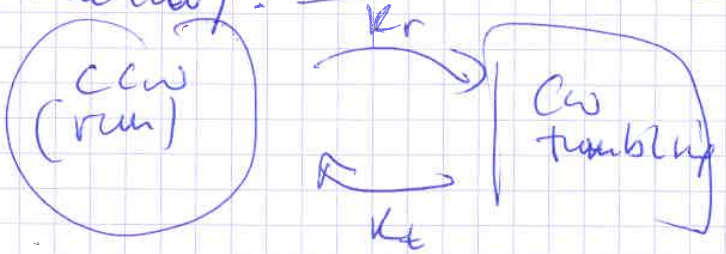
$\nu \sim 10^{-5} \frac{m^2}{s}$ (viscosity of water)

$L \sim 10\,\mu m$

run (ccw)

tumble (cw)

run & tumble



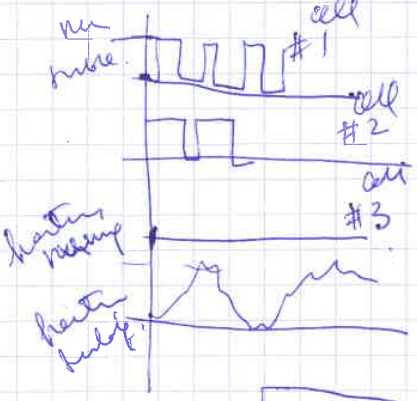
$$p_r(t+\Delta t) = p_r(t)\left(1 - P_{r\to t}\right) + p_t(t)\,P_{t\to r}$$

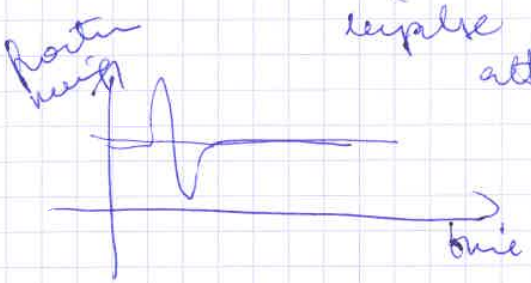
$$\left(1 - p_r(t)\right)$$

$$\frac{dp_r}{dt} \to \frac{p_r(t+\Delta t) - p_r(t)}{\Delta t} = -p_r(t)\,k_r + \left(1 - p_r(t)\right)k_t$$

$p_r(t)(-k_t - k_r) = -k_t \Rightarrow p_r = \frac{k_t}{k_t + k_r}$ at equilibrium

tethering aspirin





impulse of attractant

linear response (homogeneous).

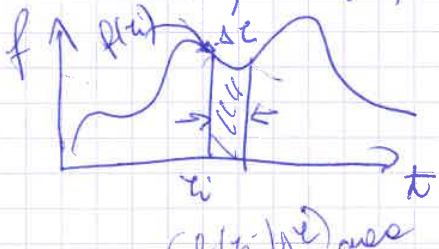
$f \Rightarrow \boxed{L} \rightarrow L(f)$ $\quad L(\alpha f + \beta g) = \alpha L(f) + \beta L(g)$

impulse $\rightarrow h(t) = \frac{1}{\tau} h_0\left(\frac{t}{\tau}\right)$

bacteria shape / function

in $\tau \to 0$ this becomes a spike and the shape does not matter.

kernel $\quad L(h) = K(t)$ we will call L a kernel.



$f = \sum_{i=0}^{N} h(t - \tau_i)\, \Delta\tau\, f(\tau_i)$

expansion of impulses

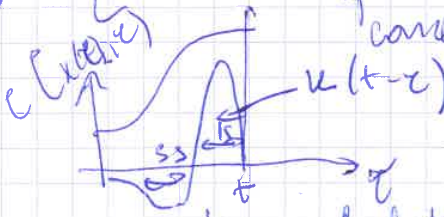
$(f(\tau_i)\Delta\tau)$ area

$L(f) = \sum_{i=0}^{N} f(\tau_i)\Delta\tau K(t-\tau)$

$\int_0^\infty f(\tau) K(t-\tau)\, d\tau$

for E. coli response $\quad p_r = \int_{-\infty}^{t_0} c(x(\tau), \tau) K(t-\tau)\, d\tau$

concentration of attractant



to calculate the response, time history of cells that run I need to convolve with a kernel

The best test cells sense gradient, comes from this kernel. Bacteria respond to what they got in the past 1s vs what they got in the last 3s:

$$c\left(\begin{smallmatrix}\text{past}\\ 1s\end{smallmatrix}\right) - c\left(\begin{smallmatrix}\text{previous}\\ 3s\end{smallmatrix}\right)$$

Is it a good idea to measure gradient in time and not space.

To see this we need to go to small Péclet #s,

ABSORB (circled)

$$\partial_t c + \bar{v}\cdot\bar{\nabla} c = D\nabla^2 c + f_c$$

(advection; diffusion; advection-diffusion eqn.)

$$\frac{UC_\infty}{L} \qquad \frac{DC_\infty}{L^2}$$

$$\frac{ADV}{DIFF} = \frac{UC_\infty}{L}\cdot\frac{L^2}{DC_\infty} = \frac{UL}{D} \qquad \left(\frac{10^{-5}\frac{m}{s}\cdot 10^{-6}\,m}{10^{-9}\,\frac{m^2}{s}} \sim 10^{-2}\right)$$

steady state no external force:

$$\cancel{\partial_t c} + \cancel{\bar{v}\cdot\bar{\nabla} c} = D\nabla^2 c + \cancel{f_c}$$

what is the diffusive flux?

$$\bar{j} = -D\frac{\partial c}{\partial r}$$

$$\cancel{\frac{1}{r^2}}\left(r^2\partial_r c\right)_r = 0$$

$$\partial_r c = \frac{A}{r^2} \qquad c = -\frac{A}{r} + C_\infty$$

$$c(R) = -\frac{A}{R} + C_\infty = 0 \qquad A = C_\infty R$$

$$c = C_\infty\left(1 - \frac{R}{r}\right)$$

$$\left.\frac{\partial c}{\partial r}\right|_R = \left.\frac{C_\infty R}{r^2}\right|_R = \frac{C_\infty}{R}$$

total flux $J = \int j\, d^3r = D\frac{\partial c}{\partial r}4\pi R^2 = -DC_\infty 4\pi R$

so it's only proportional to R, (and not to the surface).

The cell is ... the ... (cut off)

$$p(k, J, T) = \frac{(JT)^k}{k!} e^{-JT}$$ Poisson.

↑ how you cut.

$$\langle k \rangle = JT$$

$$\sigma^2 = JT \rightarrow \frac{\sigma}{\langle k \rangle} = \frac{1}{\sqrt{JT}} \sim \frac{\Delta c}{c}$$

Was it a good idea to measure gradients of the signal compared to spatial density compared to the density?

$$\frac{T \Delta c}{c} > \frac{\Delta c}{c} = \frac{1}{\sqrt{TDc 4\pi R}}$$

$\frac{vT}{R}$ velocity

$\frac{\partial_x c(R)}{c}$

see how long you have to measure T to average the errors of a perfect (Poisson) absorber

$\varepsilon \sim 10^{-6}$

for $c \sim 10^{-3} M = 1 \frac{mol}{m^3} = 6 e 10^{-23} \frac{\#mol}{m^3}$

multiply and divide by R to get ε

$$T \frac{\varepsilon^2 v^2}{R^2} > \frac{1}{4\pi RTDc}$$

↑ bacterial drift

↑ typical density taken at near points

$$T^{\#} > \left(\frac{R}{4\pi Dc v^2 \varepsilon^2} \right)^{1/3} \sim 0.75$$

$10^{-9} \frac{m^2}{s}$ $\quad 2 \frac{\mu m}{s}$

The measurement this is OK to average errors of a perfect absorber.

What about a optical measurement

$$\frac{R \partial_x c}{c} \varepsilon^2 > \frac{1}{\sqrt{T Dc 4\pi R}}$$

Brownian

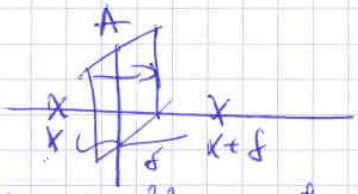
$$T > \frac{1}{\varepsilon^2 Dc 4\pi R} = 100 s$$

But this is not possible because bacteria

Interpretation of why $|J| = |-D \nabla_x 4\pi R|$

why is it proportional to R and not area.

Its because random walkers keep at close to surface.



half of the walkers at each point will go to the right and half to the left.

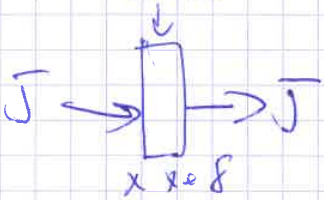
$$J = \frac{1}{2}\left[n(x,t) - n(x+\delta,t)\right] \cdot \frac{1}{A\delta\tau} =$$

$$= \frac{1}{2}\frac{C(x,t) - C(x+\delta,t)}{\delta} \cdot \frac{\delta^2}{\tau} =$$

Volume

$$= -D\partial_x C \qquad D = \frac{\delta^2}{2\tau}$$

microscopic constant of diffusion



$J(x,t) A\tau =$ [illegible]

(# of walkers that cross)

$$n(x,t+\tau) = n(x,t) + J(x,t)A\tau - J(x+\delta,t)A\tau$$

# of walkers in volume at next step.

$$\partial_t C = -\nabla j$$

If you calculate how many time a random walker hits the surface before going to infinity, that # will diverge.

So bacteria don't need to cover themselves with sticky receptors.

Lise 2 lecture 2

$\hat{n} = (\cos\theta, \sin\theta)$

The Vicsek model:

$\frac{d\vec{r}_i}{dt} = v_0 \hat{n}_i \Rightarrow$ $\vec{r}_i(t+\Delta t) = \vec{r}_i(t) + v_0 \hat{n} \Delta t$

simultaneously; for large enough [illegible] and small enough noise spontaneously [illegible],

first order & second order transitions?,

↑ very different because both [illegible] effects.

Our goal: understand transition & fluctuation / instabilities.

→ most perturbations are stable (decay quickly)

→ some decay slowly or even grow

→ develop a hydrodynamics theory for slow DOF degrees of freedom.

velocities $\omega(\vec{q}) \to 0$ as $\vec{q} \to 0$

There exist 3 ways:

1. Derive by coarse-graining a microscopic model.
2. Phenomenological: identify the relevant fields.
3. Near equilibrium entropy allowed by entropy production.

Ref. Hydrodynamics of soft active matter. Marchetti Rev Mod Phys 2013

$\omega(q) \to 0$ as $q \to 0$

1. local density of a conserved quantity
2. "Broken symmetry" – Goldstone modes: no restoring force at zero wave number.
3. Near a continuous phase transition amplitude of order parameter.

This is why useful to classify broken symmetry "polar" "nonpolar"

Momentum is not conserved, is not a slow variable for dry systems.
Wet → momentum conserved and slow variable.

For Vicsek model.

$$\rho(\vec{r},t) = \sum_n \delta\left[\vec{r} - \vec{r}_n(t)\right]$$

↑ local density

density is conserved. Birds are not being created or do not die.

order parameter $\vec{p}(\vec{r},t) = \frac{1}{\rho(r,t)} \sum_n \delta\left(\vec{r} - \vec{r}_n(t)\right) \hat{v}_n$ ← instantaneous orientation of each bird.

↑ polarization.

In thermodynamics there are two degrees of freedom that go to zero as the wave vector go to zero. You don't care about other ones.

The art is in figuring out in which terms to disregard.

Toner-Tu continuum eqn, PRL 75 1995

We want to write down an eqn for this conserved quantity,

$\frac{\partial \rho}{\partial t} + \vec{\nabla}\left(v_0 \rho \vec{p}\right) = 0$ the continuity eqn.

$\vec{p}$ plays a dual role:

- order parameter
- locally averaged velocity orientation of the flock

why this antimetagen?

and calculate the flux exited from the box

flux $\vec{J} = \rho v_0 \vec{p}$

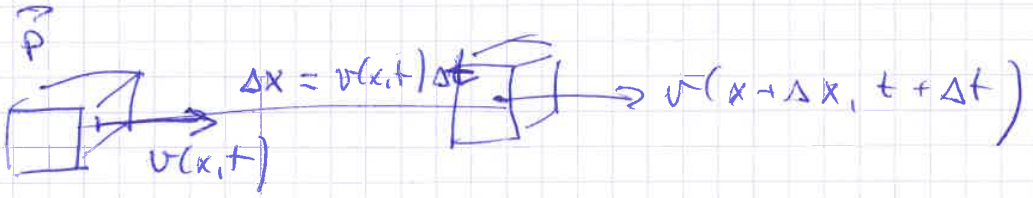
$$\frac{d}{dt}\int \rho\, dV = -\int_S \vec{J}\cdot d\vec{S}$$

change in total amount of stuff in the box

divergence theorem.

$$\frac{\partial \rho}{\partial t} + \nabla\left(v_0 \rho \vec{p}\right) = 0.$$

Next thing: write down an eqn for $\vec{p}$:



advective derivative

$$\Delta v(x,t) = \frac{\partial v}{\partial x}\left(v(x,t)\Delta t\right) + \frac{\partial v}{\partial t}\Delta t =$$

$$= \left(\frac{\partial}{\partial t} + v\frac{\partial}{\partial x}\right) v$$

this was 1D. This generalizes to a gradient in more dimensions

$$\left(\frac{\partial}{\partial t} + \vec{v}\cdot\nabla\right)\vec{v}$$

and same for $\vec{p}$

$$\left(\frac{\partial}{\partial t} + \vec{v}\cdot\nabla\right)\vec{p}.$$

There is one subtlety, what is $\vec{v}$.

It should be $v_0\vec{p}$ BUT Galilean invariance & Gross (velocity boost).

If you boost a bunch of boids moving at a constant, equal v_0, how can all boids will be moving at the same velocity, so introduce a different velocity v_i that

$$\left(\frac{\partial}{\partial t} + v_t \vec{p}\cdot\vec{\nabla}\right)\vec{p}$$

So eqn to $\vec{p}$:

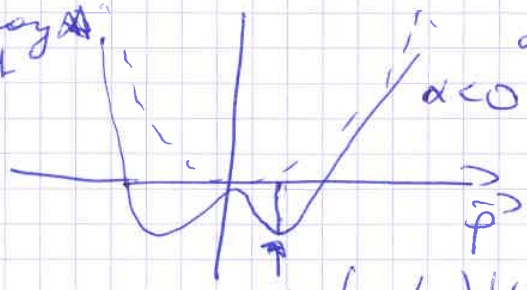
$$\partial_t \vec{p} + v_1 \left(\vec{p}\cdot\vec{\nabla}\right)\vec{p} = -\frac{1}{\gamma}\frac{\partial \mathcal{F}}{\partial \vec{p}} + f$$

← free energy. ← white noise

What kind of free energy could we write for this system? ϕ^4 theory. *

$$\mathcal{F} = \int \left[\frac{\alpha}{2}|\vec{p}|^2 + \frac{\beta}{4}|\vec{p}|^4\right] + \frac{\kappa}{2}\left(\partial_\alpha p_\beta\right)^2 + \\ - v_1 \vec{\nabla}\cdot\vec{p}\,\frac{\delta\rho}{\rho_0} + \frac{\lambda}{2}|\vec{p}|^2\,\vec{\nabla}\cdot\vec{p}$$

ϕ^4 theory * allows it



α, β tell us if I want to be in the ordered or not ordered phase.

κ - Frank free energy modulus.

for liquid crystal thing,

pseudovector term $\vec{p}\times\vec{\nabla}\times\vec{p}$ for splay, bend.

$\partial_\alpha p_\beta$ eg etc implicit summation implied.

$-v_1 \vec{\nabla}\cdot\vec{p}\,\frac{\delta\rho}{\rho_0} + \frac{\chi}{2}|\vec{p}|^2\,\vec{\nabla}\cdot\vec{p}$ couple $\vec{p}$, ρ to splay.

The derivative of the free energy:

$$\frac{\delta\mathcal{F}}{\delta\vec{p}} = -\left[-\alpha(\rho) + \beta|p^2|\right]\vec{p} + \kappa\nabla^2\vec{p} + \\ -v_1\frac{\partial\rho}{\rho_0} + \frac{\lambda}{2}\nabla|p|^2 - \lambda\vec{p}\left(\vec{\nabla}\cdot\vec{p}\right) + f$$

$\left\{+\frac{\lambda_3}{2}\nabla|p|^2 + \lambda_2\vec{p}\left(\vec{\nabla}\cdot\vec{p}\right)\right\}$ terms that are [illegible]

Analogy to Navier-Stokes

$-[\alpha + \beta|\vec{p}|^2]\vec{p}$ ~ nonlinear friction.

Symmetries ⇒ different operators:
- rotational invariance
- space + time translations
- Galilean invariance (forbids $\vec{\nabla}\cdot\vec{v}$, $\vec{v}$, $\vec{\nabla}(|\vec{v}|^2)$)

$\vec{v}$, scalar $|\vec{v}|^2$ and ρ.

"relevant" = lowest order gradients in space and time,

$$\partial_t \vec{v} + \lambda_1(\vec{v}\cdot\nabla)\vec{v} + \lambda_2(\vec{\nabla}\cdot\vec{v})\vec{v} + \lambda_3\rho\vec{\nabla}(|\vec{v}|^2)$$

if I had Galilean invariance $\lambda_2=0$, $\lambda_3=0$, $\lambda_1=1$

$$= D_1\vec{\nabla}(\vec{\nabla}\cdot\vec{v}) + D_2\nabla^2\vec{v} + D_3(\vec{v}\cdot\nabla)^2\vec{v} + \alpha\vec{v} + \beta|\vec{v}|^2\vec{v} + \nabla\rho$$

① Can this be derived for Vicsek? YES* with approximations

② What does this tell us about the system?

① ⇒ you have to make approximations about correlations functions (same weak interactions or small densities)

② mean field: density $\rho_0 < \rho_c$ then the system is isotropic.
$\rho_0 > \rho_c$ then the system is ordered
$|\vec{v}| = \sqrt{-\alpha/\beta}$

- But the Mermin-Wagner theorem (1966) (ie Chaikin-Lubensky), Hohenberg, forbids a continuous symmetry broken in 2D.

** No! Toner-Tu demonstrate with RG that although there are spurious divergences below the critical dimension ($d_c = 4$) there still exists a broader continuous RG flow (symmetry).

If you have a spin and you look at its neighbours at time t.
But if you look at time later the spin's neighbours will be different and this introduces long range correlations,
→ two apart spins can influence each other,
what are the instabilities?

① fluctuations about the isotropic core.

$$\left.\begin{aligned} \delta\rho &= \rho - \rho_0 \\ \delta\vec{p} &= \vec{p} - p_0 \end{aligned}\right\} \text{linearized eqns of motion}$$

insert into hydrodynamic eqns: ($p_0 = 0$ since we are expanding around the isotropic state)

$$\begin{cases} \partial_t \delta\rho = -v_0 \rho_0 \vec{\nabla}\cdot\delta\vec{p} \\ \partial_t \delta\vec{p} = -\alpha_0 \delta\vec{p} - \frac{v_1}{\rho_0}\nabla\delta\rho + K\nabla^2\delta\vec{p} + \vec{f} \end{cases}$$

Take a Fourier transform

$$\delta = \sum A_q e^{-i(\vec{q}\cdot\vec{r} - \omega t)}$$

similarly for $\vec{p}$ and then solve for eqn. to get

$$\omega(q) = -\frac{i}{2}(\alpha_0 + Kq^2) \pm \frac{i}{2}\sqrt{(\alpha_0 + Kq^2) - 4q^2 v_0 v_1}$$

when is the behavior of this system stable?

$$\mathrm{Im}[\omega(q)] < 0$$

linear stability ✱ > 0 positive.

this happens if & only if $v_0 v_1 > 0$

when is $v_1 v_0 > 0$ (v_0 is always > 0),

So you could get an instability of the homogeneous state

MIPS if $\sigma_i \to 0$ could get instability.

But mostly it's stable.

When are there growing fluctuations?

when $\mathrm{Re}[\omega(q)] \neq 0$

when ✱ becomes negative

when $d_0 \leq \frac{v_0 v_1}{K}$

When $d_0 \to D^+$ we approach order-to-disorder transition,

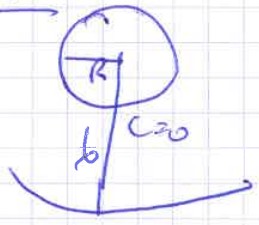
then $q \sim 2\sqrt{v_0 v_1}/K$

and then $\omega(q) \simeq \pm q \sqrt{v_0 v_1}$

this says that as you approach order to disorder transition you get a sound mode, so a propagating wave.

Aperol lecture 2

Continuous



C∞ continuous

$\nabla \sim R$

Discrete

$\partial_t p = D \nabla^2 p$

$p(x,t)$

for continuum. Pecquet $\sim R/b \hookrightarrow \langle \omega \rangle \frac{R}{b-R}$

Pecquet is the modality to be captured.

$p_\infty = 1 - p_c$

$$\langle n \rangle = \sum n p_c^n (1-p_c) = p_c (1-p_c) \sum_{n=0}^{\infty} n p_c^{n-1}$$

$$= \frac{p_c (1-p_c)}{(1-p_c)^2} = \frac{p_c}{1-p_c}$$

$1 + 2p + 3p^2 + \ldots = \frac{1}{(1-p_c)^2}$

$$= \frac{R}{b-R}$$

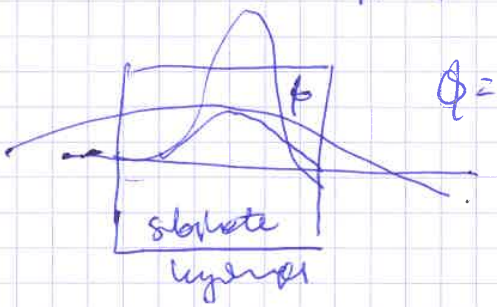
So the random walker bumps out at the boundary,

the result depends on the dimensionality of the receptor,

Biofilm

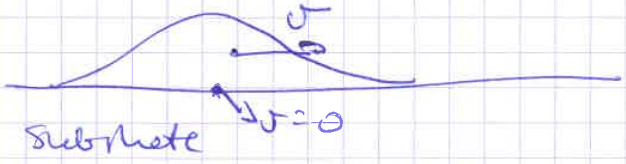
Biofilm most like gels.

Two fluid mixture + slow deposition then equilibrium + thin film + self similar solution.



ϕ = volume fraction polymer,

$\phi + \delta\phi$



no slip condition because there is friction,

what forces make them expand,

ϕ : volume fraction of the bacteria $\rightarrow \bar{v}_b(\bar{x}, t)$

$1-\phi$: volume fraction of water. $\rightarrow \bar{v}_w(\bar{x}, t)$

$$\omega + \dot{F} = \left(\left[\frac{\xi}{2} \| \bar{v}_w - \bar{v}_b \|^2 - \bar{v}_b \left(\nabla \cdot \bar{\bar{\sigma}}_w \right) - \bar{v}_w \left(\nabla \cdot \bar{\bar{\sigma}}_w \right) \right. \right.$$

friction between water and bacteria

continuity of biomass and water:

$$\begin{cases} \partial_t \phi_b + \vec{\nabla} \cdot (\phi_b \vec{v}_b) = g \leftarrow \text{growth rate source of biomass} \\ \partial_t \phi_w + \vec{\nabla} (\phi_w v_w) = -g \end{cases}$$

same as $1-\phi$ } kept to make it clear.
same as ϕ below

Its an effective description. There should be two eqns: one for bacteria + 1 for polymers. Bacteria are producing biomass, polymers are not. Here we put it together.

$\Rightarrow$ sum $\quad \partial_t (\phi_b + \phi_w) + \nabla (\phi_b \vec{v}_b + \phi_w \vec{v}_w) = 0$

$\phi + 1 - \phi = 0$

so $\boxed{\vec{\nabla} \cdot \vec{v} = 0}$ for $\vec{v} = \phi_b \vec{v}_b + \phi_w \vec{v}_w$

so its incompressible

$$W + \dot{F} = \int \Big[\frac{\xi}{2} \| \vec{v}_w - \vec{v}_b |^2 - \vec{\sigma}_b (\vec{\nabla} \cdot \vec{v}_b) - \vec{\sigma}_w (\nabla \cdot \vec{v}_w) +$$
$$- p \Big[\nabla \left(\vec{v}_b \cdot \phi + \vec{v}_w (1-\phi) \right) \Big] + \frac{\partial f}{\partial \phi} \left(g \cdot \vec{\nabla} \cdot (\phi \vec{v}_b) \right) \Big)$$

$\phi_b = \phi \quad \phi_w = 1 - \phi$

Take derivatives with respect to v_b and v_w:

$\frac{\partial}{\partial v_w}$: $\xi (v_w - \vec{v}_b) - (\nabla \vec{\sigma}_w) + (1-\phi) \vec{\nabla} p = 0 \qquad (1)$

$\frac{\partial}{\partial v_b}$: $\xi (v_b - \vec{v}_w) - (\nabla \cdot \vec{\sigma}_b) + \phi \vec{\nabla} p + \underbrace{\left(\nabla \frac{\partial f}{\partial \phi} \right) \phi}_{\nabla \pi} = 0 \qquad (2)$

osmotic pressure:

$\pi = \frac{\partial f}{\partial \phi} \phi - f$

we assume that both water & the biofilm are non-newtonian fluids (no memory in opposite to perturbation non-newtonians quiet):

$$\bar{\nabla} \cdot \bar{\bar{\sigma}}_w = \mu_w \nabla^2 \bar{v}_w$$

$$\bar{\nabla} \cdot \bar{\bar{\sigma}}_b = \mu_b \nabla^2 \bar{v}_b$$

SUM (1) & (2)

$\mu_b \nabla^2 \bar{v}_b = \bar{\nabla} p + \bar{\nabla} \bar{\bar{\Pi}}$ the Stokes eqn,

$\bar{v}_w = \bar{v}_b - \frac{(1-\phi)}{\xi} \bar{\nabla} p$ DARCY eqn,

Either substrate thin or fog and that a small parameter

→ thin film model.

natural small parameter,

$h/R \ll 1$ expand.

$\bar{\nabla} \cdot \bar{v} = 0 = \partial_x u + \partial_y v \Rightarrow u \gg v$

$\frac{u}{R} \quad \frac{v}{h}$

in typical thin film models.

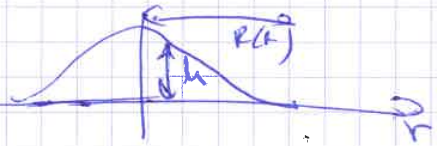
but we cannot do this since we have growth

but otherwise it's a classic thin-film model calculation.

Black box thin film model.

↓

you end up with an eqn for $h \rightarrow$ biofilm height



$\partial_t h - k \frac{P}{r} \partial_r \left[h^3 \partial_r h \right] = g h$

$h(r,t)$ = shape of biofilm

assuming cylindrical symmetry

(we assume it depends on distance from the center and on time),

if $k \neq 0$ $h \sim \exp(t)$ so no symmetry,

The κ term is a flux.

This is a nonlinear diffusion eqn.

with $D(h) = \frac{\kappa R}{r} h^3$

$h = H e^{\gamma t}$ $\quad h_t - \kappa \frac{R}{r} (h^3 h_r)_r = \gamma h$ $\qquad$ wrt. $h_r = \frac{\partial h}{\partial r}$, $h_t = \frac{\partial h}{\partial t}$

$H_t = \kappa \frac{R(t)}{r} (H^3 H_r)_r e = 0$

$R(t)$ ← radius of biofilm. $R(t)$ depends on h.

eliminate $R(t)$ explicitly.

define $H_\tau = H_t R e^{3\gamma t} \kappa$

$H_\tau \cancel{R e^{3\gamma t} \kappa} + \cancel{\frac{\kappa R e^{3\gamma t}}{r}} (r H^3 H_r)_r = 0$

$H = \frac{1}{R(\tau)^2} F\left(\frac{r}{R(\tau)}\right)$ self-similarity.

$\int_0^\infty H 2\pi r \, dr = \int_0^\infty \frac{1}{R^2} F\left(\frac{r}{R(\tau)}\right) 2\pi r \, dr =$

$= \int F(\xi) \, \xi 2\pi \, d\xi$ $\qquad r/R = \xi$

we've separated the space ξ and the dependent $R(\tau)$

go back to the eqn.

$-2\frac{\dot R}{R^3} F + \frac{1}{R^2} F'\left(-\frac{r}{R^2}\dot R\right) - \frac{1}{r}\left(r \frac{F^3}{R^6} \frac{F'}{R^2}\frac{1}{R}\right)' \frac{1}{R} = 0$

$F' = \frac{\partial F}{\partial \xi}$ $\quad \xi = \frac{r}{R}$ $\quad \dot R = \frac{\partial R}{\partial \tau}$

$\frac{1}{R}\frac{\partial F}{\partial \xi} = \frac{\partial F}{\partial r}$

$\frac{1}{R^3}\left(2\dot R F \; \dot R F' \xi\right)$

$\dot R \left(2F \;\; F'\xi \right) \quad 1/(\xi F^3 F')'$ $\qquad$ it worked because we eliminated

So now apply to L:

$\frac{\partial R}{\partial t} = \frac{1}{R^7}$ solved.

so $\frac{\partial R}{\partial t} = \frac{\pi e^{3\rho A} K}{R^{7-6}} \Rightarrow \frac{R^7}{7} = \frac{e^{3\rho A} K}{3\rho} + \text{constant}$

R will start content out then if the shell becomes large enough it will grow.

So it holds the

First it goes up and then it spreads.

Eleni lecture 2

Reminder

$\langle \hat{\Delta} \vec{f}, \vec{\tau} \rangle = \langle \vec{f}, \hat{\Delta}^T \vec{\tau} \rangle$ *

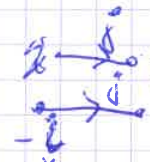
$\vec{\tau}$: $M \times 1$ vector defined on ordered links, $\vec{e}$, $e_j > 0$

$\vec{f}$: $N \times 1$ vector defined on ordered nodes, $\vec{q}$, $\vec{p}$

q_j flow

$\hat{\Delta}^T$ $N \times M$ incidence matrix

$\hat{\Delta}_{ij}^T = \begin{cases} 1 \\ -1 \\ 0 \end{cases}$



$q_j = C_j (p_i - p_j)$

$C = \frac{\pi R^4}{8 L \mu}$

$Q = -\text{diag}(\vec{C}) \hat{\Delta} \vec{p}$

Where does the sign come from $\vec{p_1} \rightarrow \vec{p_2}$

$\hat{\Delta} \vec{p} < 0$ if $Q_{12} > 0$

$\vec{i} = \vec{Q}$ ← flow — How much energy it takes to push the blood through the system.

$\vec{f} = \vec{p}$ ← pressure.

$\langle \Delta\vec{p}, \vec{Q} \rangle = \langle \vec{p}, \Delta^T \vec{Q} \rangle \Rightarrow \Delta p_i'$

$\Rightarrow \langle \Delta\vec{p}, \vec{Q} \rangle = \langle \vec{p}, \vec{q} \rangle$

$\Delta\vec{p}$: pressure difference at every link; $\vec{Q}$: current at any link

$\sum \left(-(p_i' - p_j) Q_{ij}' \right) = \sum p_i' q_i'$

$\Rightarrow \sum_{ij} (p_i' - p_j) Q_{ij}' = -\sum_i p_i' q_i'$

$\mathbb{P}$ power dissipated (also $\Delta V \cdot I$ or $\Delta E / t$) at individual link in the body

$\mathbb{P} = -\sum_i p_i' q_i'$

what is $p_i' q_i'$?

the heart

closed system

any current in the body

$q_i' = (-\delta_{i1} + \delta_{iN}) q_0$

↑ cardiac output 5L/min

$\mathbb{P} = (p_1 - p_N) q_0$

p_1: 90 mm Hg ≈ 12000 Pa ≈ 8700 kJ

Another example

$\vec{i} \to \vec{Q}$ $\quad \vec{f} = \begin{bmatrix} \\ \\ \end{bmatrix}$ $N \times 1$

Back to * identity

$LHS = \langle f, \Delta^T \vec{Q} \rangle = \langle \vec{f}, \vec{q} \rangle = \sum_i q_i'$

$RHS: \Delta f = \sum_j \Delta y_j = \sum \Delta T_{or}' = 0$

$RHS: \langle \Delta\vec{T}, \vec{i} \rangle = \sum \Delta T_i' i_i' = 0$ $\Rightarrow \sum_i q_i' = 0$ net current

What is $\vec{Q}$ if you know $\vec{q}$, $\vec{C}$?
How much flow goes to every vessel?

You can go to the eqns we've proven

$$\left.\begin{aligned} \vec{Q} &= -\,\mathrm{diag}(\vec{C})\,\hat{\Delta}\vec{p} \\ \hat{\Delta}^{\top}\vec{Q} &= \vec{q} \end{aligned}\right\} \qquad \left(\begin{aligned} I &= \frac{V}{R} \\ \textstyle\sum_i I_i &= q \end{aligned}\right)$$

You have two unknowns $\vec{Q}$ and $\vec{p}$.

Eliminate $\vec{p}$:

$$\hat{\Delta}^{\top}\vec{Q} = -\,\hat{\Delta}^{\top}\,\mathrm{diag}(\vec{C})\,\hat{\Delta}\vec{p}$$

$$\underbrace{\hat{\Delta}^{\top}\,\mathrm{diag}(\vec{C})\,\hat{\Delta}}_{\hat{L}}\,p = -\vec{q}$$

$\hat{L} = \hat{\Delta}^{\top}\,\mathrm{diag}(\vec{C})\,\hat{\Delta}$ Laplacian matrix.

You can show: $\hat{L} = \begin{bmatrix} \sum_{ik} C_{ik} & -C_{12} & -C_{13} & \\ -C_{12} & \sum_{ik} C_{ik} & & \\ -C_{13} & & \ddots & \\ & & & \end{bmatrix} = \hat{A} - \hat{C}$

(adjacency matrix − diagonal elements)

$\hat{L}$ is a symmetric matrix.

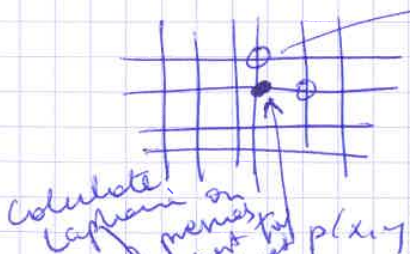
This matrix has a feature $\sum_i L_{ij} = 0$

it has at least one zero eigenvalue.

$\Rightarrow$ its not invertible.

You have another Laplacian ∇^2.

$\hat{L}$ is a discrete version of ∇^2.



assume all conductances are constant

$$\left[\hat{L}\vec{p}\right]_{x,y} = 4C\,p(x,y) - C\left(p_{x,y+\Delta y} + p_{x,y-\Delta y} + p_{x+\Delta x,y} + p_{x-\Delta x,y}\right) = \ldots$$

← Laplacian

$\hat{L}\vec{p} = -\vec{q} \Rightarrow$ $\boxed{\nabla^2 p(x,t) = \frac{1}{c(\Delta x)^2} q(x,t)}$

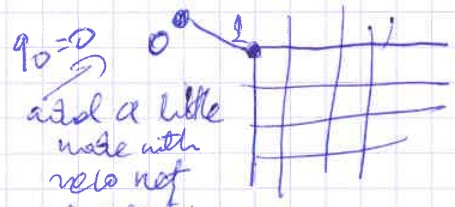
Poisson eqn.

$\hat{L}\vec{p} = -\vec{q} \Rightarrow \vec{p} = -\hat{L}^{-1}\vec{q}$

Its not invertible because pressure (like voltage) is defined up to a constant (you increase the pressure everywhere in your system and it will not change anything).

But you can take the pseudo inverse of $\hat{L}^{-1}$

How to invert it: $L_{11} \Rightarrow L_{11} + \epsilon$ add a constant



set $p_0 = 0$

So now we can calculate the current for any C:

$\vec{Q} = \underbrace{\text{diag}(C)\,\hat{A}\hat{L}^{-1}\vec{q}}_{\text{computed function of } \vec{C}}$ ← boundary current

Which network architecture is better and under which constraints?

OPTIMIZATION

what to minimize? dissipation in animals?
power lost due to friction.

P dissipation (animals)

for plants $\frac{1}{N}\sum_i (p_i - p_0)$ average pressure drop

keeping $\vec{q}$ constant $C \to \infty$ as $c_{ij} = c_{ij}(p_i - p_j)$

conductances cost:

Paper by Cecil D. Murray 1926 on physiological principle of minimal work.

↳ Murray's law.

For laminar flow $C = \frac{\pi R^4}{8L\mu}$

The cost to build a vessel could be by the volume, the area or the length.

Assume that the cost per vessel is proportional to the surface area of the vessel

$k \sim 2\pi RL$ (proportional to area).

$\sim (CL)^{1/4} L$

If I double the conductance, the cost goes up by $C^{1/4}$

Now by volume $k \sim \pi R^2 L \sim (CL)^{1/2} L$

So it seems you are better off paying by the area. Unfortunately, at least according to Murray, you pay by the volume. Because you maintain the flow and displace tissues.

from Murray $C = \frac{\alpha R^4}{L}$

$P = Q \Delta P = \frac{Q^2}{\alpha R^4} L$ ← power

vessel cost proportional to volume $k = \beta L \pi R^2$

Minimize total rate of energy loss

$E = P + k = \left(\frac{Q^2}{\alpha R^4} + \beta \pi R^2 \right) L$

$\varepsilon = E/L$ ← power

$\frac{d\varepsilon}{dR} = 0 \Rightarrow \beta = \frac{2Q^2}{\alpha \pi R^6} \Rightarrow \frac{Q^2}{R^6} = k^2 \Rightarrow Q = kR^3$

Lets imagine I have a mother vessel ——— Murray's law

Whenever things bifurcate the sum of the radiuses cubed is constant

ALLOMETRY IN BIOLOGY

allometry ⇒ mass of organism increases one thing changes how things scale with mass?

Perfectly isometric organism, $V = M$

$A \sim M^{2/3}$

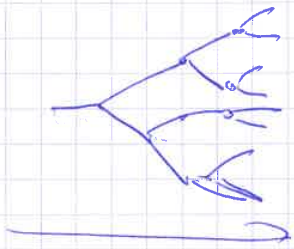
$L \sim M^{1/3}$

Basal metabolic rate follows $B \sim M^{3/4}$

People were trying to really explain it,

There is a paper that may be wrong and the data may be wrong, but the arguments are interesting ⇒ It explains that the scaling of $B \sim M^{3/4}$ comes from vascular system.

They assume the vascular system is a fractal branching system



n_k - number of branches each vessel splits to.

$N_k = \prod_{i=0}^{k} n_i$

N - total # of generations

k generations

at each generation N_k vessels.

cardiac output $Q_0 = N_k Q_k = N_c Q_c$ ← flow at the capillaries, at the capillaries,

Q_0: heat output; $N_k Q_k$: at each generation

$B \sim Q_0 N_c = N_c \pi r_c^2 v_c^2 \sim N_c \sim \langle n \rangle^N$ (4)

B: basal metabolism; N_c: # of capillaries; $\langle n \rangle$: average bifurcation rate

Heat rules output since the heart is your blood circulates you have the most support

Self similarity argument?

$\beta = \frac{r_{k+1}}{r_k}$ ← ratio of radii of cat each node.

$\gamma = \frac{l_{k+1}}{l_k}$ ratio of lengths at each point

$n_k = n$ ← bifurcation rate is const.

assume $M \sim V_b$ total mass proportional to the blood volume.

$$M \propto \sum_{k=0}^{N} N_k V_k = \sum_{k=0}^{\infty} \pi r_k^2 l_k n^k = \dots = n^N V_c \frac{(n\gamma\beta^2)^{-N+1} - 1}{(n\gamma\beta^2)^{-1} - 1}$$

Assume $N \gg 1$ (a lot of points).

$n\gamma\beta^2 < 1$ => means that the total vessel volume decreases at each generation

$$M \sim V_c \frac{(\gamma\beta^2)^N}{1 - n\gamma\beta^2} \quad (1)$$

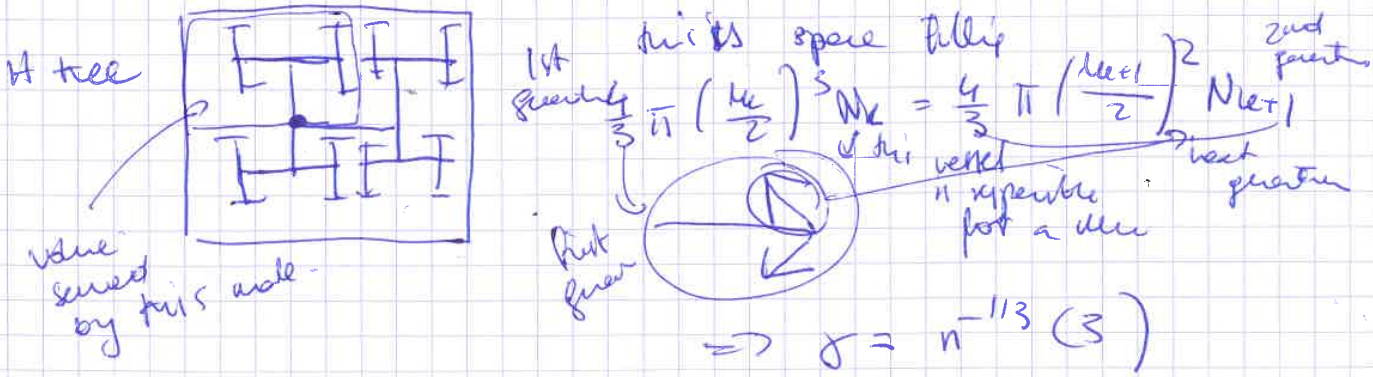
we don't know β? (2)

They use area preserving branching $\beta = n^{-1/2}$

What is γ?

This will introduce us to a space filling graph.

You make successive H's;



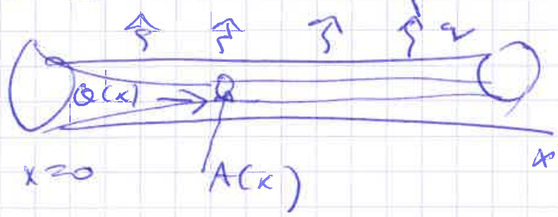
$$\Rightarrow \gamma = n^{-1/3} \quad (3)$$

We can now collect eqns 1-4:

(4) $B \sim n^N$ ∴ $\frac{1}{2} R \sim M^{3/4}$

More concrete problems about optimization in leaves

spherical cow of a leave; pure veinlet



conductance in a leaf minimizes pressure drop.

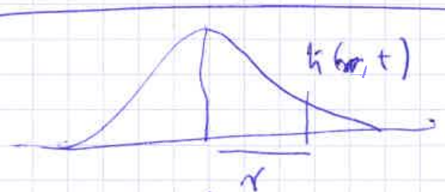
$k \sim C^{r}$ which one is better?

Agenda
lecture 3

continuing with biofilms, back to eqn.

$$\partial_t h - k \frac{\rho}{r} \partial_r \left[r h^3 \frac{\partial h}{\partial r} \right] = g h$$

thin film diffusion eqn nonlinear for biofilm.



$h = H e^{gt}$

$H_\tau = H_t \frac{Rk e^{3gt}}{dt}$ ← implicit

we found the solution for R:

$$R/R_0 = \left[1 + \frac{7k}{3g} \left(e^{3gt} - 1 \right) \right]^{1/7}$$

dependence on time.

$H = \frac{1}{R^2} F\left(\frac{r}{R}\right)$, $\frac{r}{R} = \xi$

going back to last lecture's notes:

[illegible]

$\xi^{2}/\!\!\not{F} = - \not{\xi} F^{\not{3}2} F' + \not{6} = 0$ $\qquad F_{BC}(\xi = 0) = 0$

$F^2 F' = -\xi$

$\frac{F^3}{3} = -\frac{\xi^2}{2} + \text{const}$

↓ c' fixed by the mean of the profile by mass concentration.

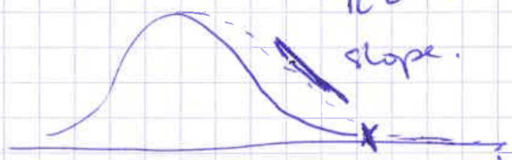
self-similar solution

$$F = \left[C - \frac{3}{2} \left(\frac{r}{R(t)} \right)^2 \right]^{1/3}$$

dependence on space

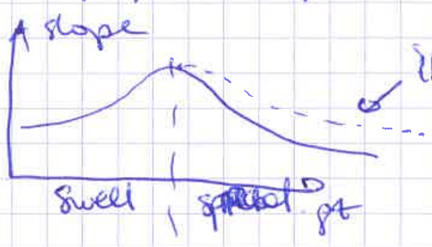
Both give the full solution.

So $h(r,t) = \frac{e^{gt}}{R^2} \left[c - \frac{3}{2} \left(\frac{r}{R} \right)^2 \right]^{1/3}$



the LST shows the swelling / spreading transition

$h(\infty) \sim h_\infty(t=0)\, e^{gt}$



If h_∞ = constant different BC

what is wetting?

more interface liquid - vapour.

more interface liquid-solid

Which one will happen depends on the free energy of creating there liquid-solid or vapour-solid interface.

$$K = \frac{1}{2(1-\phi_\infty)^2} \frac{\mu_w}{\mu_b} \frac{h_0^3}{\xi_\infty^2 R}$$

↓ biomass volume fraction

↘ biomass work give at

TURBULENCE PRIMER

energy injection (e.g. at the atmosphere)

$$\partial_t \bar{v} + \bar{v}\cdot\bar{\nabla}\bar{v} = \nu\nabla^2\bar{v} - \frac{1}{\rho}\bar{\nabla}p + \bar{f}$$

Navier-Stokes eqn.

$\frac{|v^2|}{2}$

$Re = \frac{UL}{\nu}$ $\quad Re \gg 1$ turbulent

$Re \lesssim 1$ laminar (diffusive)

η Kolmogorov scale. $\quad L \leftarrow$ integral scale.

energy is dissipated.

energy is injected.

Turbulence is injecting energy at large scales and dissipating it at small scales. (It is the transfer of energy.

Do dimensional reduction,

assume ε const

$$\Rightarrow * \quad \frac{v_r^3}{r} = \varepsilon \Rightarrow \text{energy dissipation rate.}$$

@ $r = \eta$ $\quad \frac{v_\eta^3}{\eta} = \nu\frac{v_\eta^2}{\eta^2}$ (1)

$$\frac{v_\eta^3}{\eta} = \varepsilon \qquad (2)$$

(1) + (2) $\Rightarrow$ $\eta = \nu^{3/4}\varepsilon^{-1/4}$

$$\frac{L}{\eta} = \frac{v_L^3}{\varepsilon L}\left(\frac{L}{v_\eta}\right)^3$$

3D Homogeneous isotropic turbulence

v_r – velocity difference at a scale r.

$v_r = \langle |\bar{v}(\bar{x}+\bar{r}) - \bar{v}(\bar{x})|^2 \rangle^{1/2}$ typical fluctuations at the scale r

$$\frac{L}{\eta} = \left(\frac{u}{v_\eta}\right)^3 = \left(\frac{u}{v^{1/4}\varepsilon^{1/4}}\right)^3 = \left(\frac{u}{v^{3/4}\varepsilon^{3/4}}\right) = \left(\frac{uL}{v}\right)^{3/4}\left(\frac{u^{3/4}}{\varepsilon^{3/4}L^{3/4}}\right) = Re^{3/4}$$

$\left(\frac{u^{3/4}}{\varepsilon^{3/4}L^{3/4}}\right) \to 1$

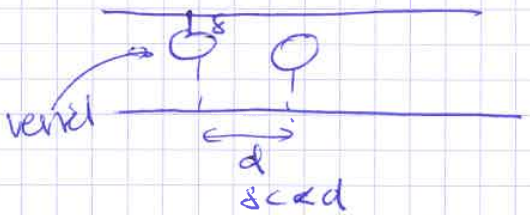
$\eta = \varepsilon^{1/4} v^{3/4}$

$v_\eta = \varepsilon^{1/3}\eta^{1/3} = v^{1/4}\varepsilon^{1/4}$

$\frac{v_\eta^3}{\tau} = \varepsilon$

Eleni lecture 3

Optimal vein density



total flux:

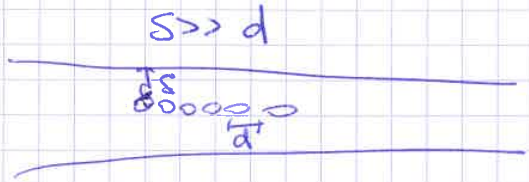
single vessel flux

$j \sim D(c_0 - c_1)\frac{\delta}{d}$

$J \sim jN = j\frac{W}{d}$

$\Rightarrow J \sim D\frac{(c_0 - c_1)W}{d\delta}$

In the opposite regime:



$J \sim \frac{D(c_0 - c_1)}{\delta} W$

So $d \sim \delta$ → it when there two scales cross.

optimality of leaky pipes

Rule of five models

Flow conservation eqn:

$$Q(x+\Delta x) - Q(x) = -q\Delta x$$

boundary condition $Q(L) = 0$

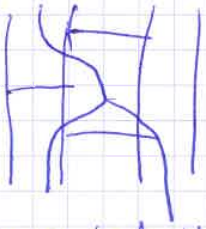
(the leaf has exhausted all the water)

$Q(x) = q(L-x)$ ← flow drops linearly along

how does this 1D pipe operate? 1D leaf.

$\Delta p = \frac{Q}{C}$ not right

But we have the problem that this is a porous medium.



So it's no longer flow but more of a percolation.

So we should be using Darcy's law

$$u(x) = -\frac{k}{\mu}\frac{dp}{dx}$$

k → permeability, μ → viscosity

To find about Darcy's law:

Go back to $\Delta p = \frac{1}{C}\Delta Q$ how much flow you can have for a given pressure drop.

$A(x)$ - cross sectional area of the pipe.

$$A(x)u(x) = -\frac{kA(x)}{\mu}\frac{dp}{dx} \Rightarrow \Delta p = \left(A(x)u(x)\right)\left(\frac{\Delta x}{kA(x)}\mu\right)$$

$$\Delta p = Q\left(\frac{\Delta x}{kA(x)}\mu\right)$$

this is like resistance, how good or bad resistance it is.

$$\Rightarrow \frac{dp}{dx} = \frac{-\mu q(L-x)}{kA(x)}$$

I want to minimize pressure drop.

This can happen by saying $A(x) \to \infty$ but this is too expensive.

$A(x) \sim N(x) \Gamma \sim K R$ ← $N(x)$ models per unit length. ← how much the plant is willing to invest.

So optimize pipe cost.

q = fixed we assume that: $\int_0^L A(x)\,dx \sim \int_0^L N(x)\,dx \le K$ Lagrange ln.

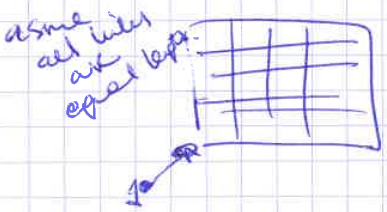
$\tilde{x} = \frac{x}{L}$

$\tilde{C} = \int \frac{1}{N(\tilde{x})} d\tilde{x} + \lambda \int N(\tilde{x})\, d\tilde{x}$

$N(\tilde{x}) = N_0 \sqrt{1-\tilde{x}^2}$

Optimal topology

N nodes.



$q_i' = -\delta_{ij} q + (1-\delta_{ij}) \frac{q}{N-1}$

what is the cost of each pipe?

pipe needle $K \sim A \sim R^2$

$\frac{dp}{dx} = -\frac{\mu J}{K} \Rightarrow \dots \Rightarrow C \sim R^2$ } $K \sim C$

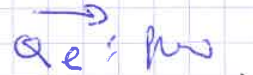
Poiseuille flow: $C \sim R^4$ if $K \sim R^2$ } $K \sim C^{1/2}$

no slip boundary condition means zero velocity at the vessel wall, so you get a logged flow.

IN general $k \sim C^{\gamma}$ cost.

minimize $\tilde{C} = \sum_e \frac{q_e^2}{c_e} + \lambda \sum_e c_e^{\gamma}$

$K = \sum_e c_e^{\gamma}$



q_e: flow

c_e: conductance

K: total cost.

$\gamma > 1$: convex → unique minimum

$\gamma < 1$ non-convex → multiple local minima

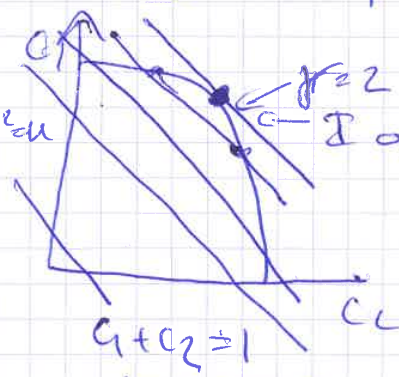
best of the envelope argument for why γ is important

$q_1 + q_2 = q_0$

$\min(E) = \min \sum c_e^2 \frac{1}{(C_1+C_2)} \Rightarrow \min\left(\frac{1}{C_1+C_2}\right) \rightarrow \max(C_1+C_2)$

$\sum C^\gamma = C_1^\gamma + C_2^\gamma = K$

for $\gamma = 2$ it's a circle $C_1^2 + C_2^2 = K$



I optimally satisfy the constraint but it's a triple point.

these do not hit the constraint so they are not allowed solutions

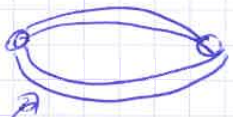
If I had a 4 dimensional problem → do it merely find a triple point.

optimal, two points. C_2 gets all the congestion but C_1 gets nothing.

one point but not optimal.

What this means for this graph is

$\gamma > 1$

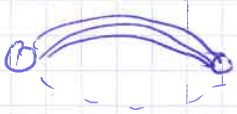


small pipes are cheap large pipes are very expensive

both pipes are used

You distribute your congestion

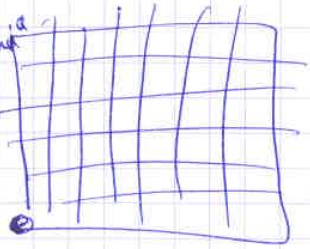
$\gamma < 1$

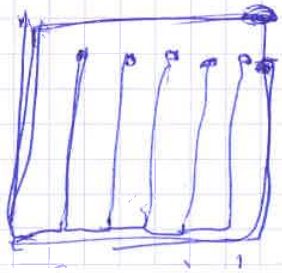


one pipe disappears and the other one gets all the congestion.

large pipes are only slightly more expensive than small pipes

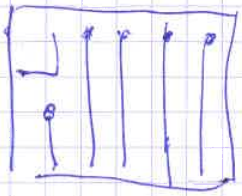
many different more complicated networks





no loops,

→ many local minima. Any spanning tree will be a tree that



← other spring likes.

optimal to plug

$$\vec{e} = + \text{diag}(c)\, \hat{s}\, \hat{L}^{-1}\, \vec{q}$$

Imagine that $\vec{q}$ is not always the same.
It doesn't always have the same demands.

fluctuations $\{\vec{q}\}$

$\langle \vec{e} \rangle = \ldots \langle \vec{q} \rangle$

$$E = \sum \frac{e^2}{2c}$$

$$E = \sum \frac{\langle e^2 \rangle}{2c}$$

~~Redundancy~~ Damage

a damage close to the root can cause great damage to the network.

tree like networks are not robust.

$p_c = \frac{1}{M}$ prob of damage

↑ probability of removing an edge

you can look at it relatively.

Modern cities have lateral connections which are more robust to damage.

Gingko leaves are very ancient, have a tree like structure and they cannot transmit water past damaged sites.

Just because it optimal it does not mean nature can build it. So we have to worry about development.

Two major modes of development: ~~growth~~ tip growth and ~~remodeling~~ both remodeling

Use lecture 3

Interactions II : steric interactions

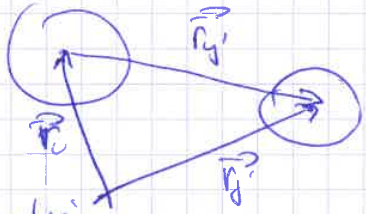
Focus first on particles with spherical symmetry.

→ no alignment due to steric effects.

1. Interactions

V_{ij}

$V_{ij} = V(|r_i - r_j|) = V(r_{ij})$



Lennard-Jones:

$$V(r_{ij}) = 4\varepsilon\left[\left(\frac{\sigma}{r_{ij}}\right)^{12} - \left(\frac{\sigma}{r_{ij}}\right)^{6}\right]$$

steric repulsion ← $\left(\frac{\sigma}{r_{ij}}\right)^{12}$ — $\left(\frac{\sigma}{r_{ij}}\right)^{6}$ → attractive

This exponent varies but it is often between 12 and 6

This is always 6 because of VdW interactions (dipoles)

Focus on potential that only has repulsion:

$$V(r_{ij}) = \begin{cases} \varepsilon \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{\alpha} & r_{ij} > 0 \\ 0 & \text{otherwise} \end{cases}$$

σ_{ij}

2. Add activity or self-propulsion

$$m\frac{d\vec{v}_i}{dt} = \vec{F}_{int} + \vec{F}_{sp} + \vec{F}_{drag} + \vec{F}_{work}$$

overdamped

$$\sum_j -\frac{\partial V(r_{ij})}{\partial r_i} + F_0 \hat{n}_i - \sum \sigma_i$$

$\mu \leftarrow$ mobility (just notation)

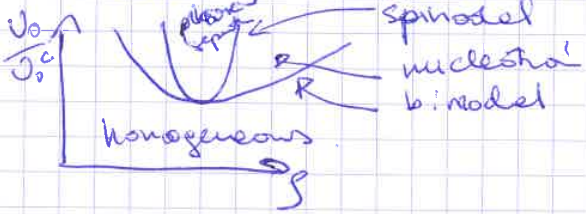
$$\frac{dr_i}{dt} = \frac{F_0}{\xi}\hat{n}_i - \left(\frac{1}{\xi}\right)\sum \vec{J}_i V(r_{ij})$$

people do μn_i

$$\dot{r}_i = v_0\hat{n} - \mu \sum_i J_i V(r_{ij}) \qquad \dot{\theta} = \eta$$

Motility induced phase seperation

Cates & Tailleur Annual Review of Condensed Matter Physics (2015)



Glassy dynamics / Jamming.

at high densities you get a different transition

$$\phi = \sum_i \frac{\pi \sigma_i^2}{R^2}$$

ϕ: packing fraction; $\pi\sigma_i^2$: area of disks; R^2: area

δ-number density per volume

Motility Induced Phase Seperation (MIPS)

Those are purely repulsive particles why do they stick together,

These particles stick together for a time ~ persistence time self propulsion

+ higher densities

→ more opportunities for collisions.

→ [illegible]

Expect $\nearrow Pe$ = more MIPS Pe - Péclet number
sweet spot in ρ, ϕ where this effect is enhanced.

(2) Hydrodynamic model
→ no interactions b/w spins just steric
→ what is left from our hydro theory?
no $\vec{\nabla}\cdot\vec{p}$, $|\vec{p}^2|$, $(\vec{v}\cdot\vec{\nabla})\vec{p}$
We can have $\nabla\rho$, $\vec{p}$
new ingredient: $v_0 \neq \Rightarrow v(\rho)$
↑ interactions change our velocity.

$$(1) \quad \partial_t \rho = -\nabla[v(\rho)\vec{p}]$$
$$(2) \quad \partial_t \vec{p} = -D_r \vec{p} - \tfrac{1}{2}\nabla[v(\rho)\rho]$$
$$v(\rho) = v_0(1 - \lambda\rho)$$
virial expansion

Take an adiabatic approximation.
At $t \gg \frac{1}{D_r} \Rightarrow \vec{p} = -\frac{1}{2D_r}\nabla[v(\rho)\rho]$ ← $\frac{\partial v}{\partial \rho}$
$$\Rightarrow \partial_t \rho = \vec{\nabla}\cdot\left[\underbrace{\frac{v(\rho)^2 + \rho v(\rho)v'(\rho)}{2D_r}}_{D(\rho)}\nabla\rho\right]$$

When $D(\rho) < 0$ then diffusion
but when $D(\rho) > 0$ you can get an instability.
So when does D change sign.
$v' < 0 \Rightarrow D(\rho)$ changes sign
$$v(\rho) < -\rho v'(\rho)$$
At high ρ
You want to calculate the binodal & the spinodal,
[illegible]

From this we can calculate the spinodal when $p=0$ etc.

Takatori & Brady PRE 2015

Yang, Manning, Macklethi 2014

Yang PNAS 2017

A. Two contributions to pressure ← in active matter systems

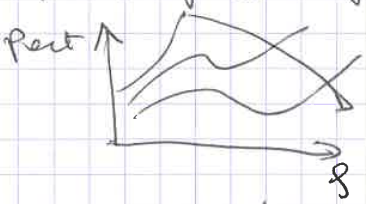
- an active "swim" pressure, describes the flux of momentum / force $\frac{V_0}{\mu} \hat{n}_i$ across a boundary. (propulsive force while these particles are self-propelled)

$$\sigma_{\alpha\beta}^{i\,(swim)} = -\frac{V_0}{\mu A_i} n_\alpha^i r_\beta^i$$

interaction pressure

$$\sigma_{\alpha\beta}^{i\,(int)} = \frac{1}{2} \sum_{j \neq i} f_{ij} r_{ij} \frac{x_i y_j}{r_{ij}^2}$$

total pressure p^{act} is sum over σ^{int} and σ^{swim}.

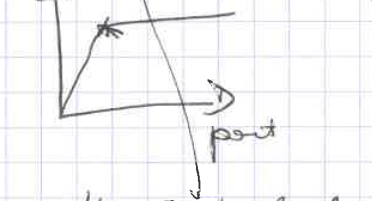


$$Pe = \frac{V_0}{2RD_r}$$

$\frac{\partial p^{act}}{\partial \rho} = 0$ is spinodal.

binomial: chemical potential is same in dense + dilute region

but it is not always (for example dense + low density electrons)



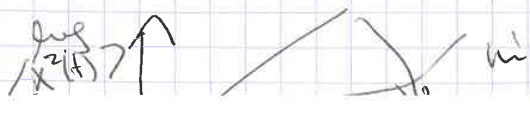
$$n\left(\frac{\partial \mu^{act}}{\partial n}\right) = (1-\rho)\frac{\partial p^{act}}{\partial \rho}$$

n: number density; μ^{act}: chemical potential; p^{act}: thermodynamic equation of state

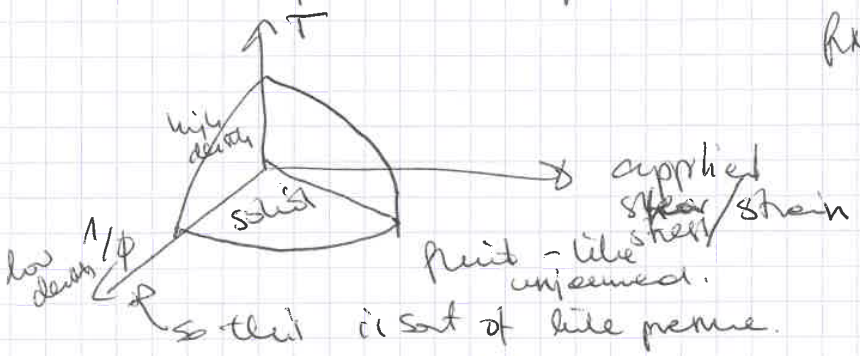
We made up pressure and it reproduces the spinodal.

Jamming $V(\rho) = V_0(1-\rho)$ ← breaks down at high densities

→ system becomes solid like, particles don't change neighbours → get stuck in a cage.



Jamming phase diagram



So this is sort of like pressure.

real world.

There is some density of pennys at which I become rigid.

I can unjam a penny system by a shear system (they will change their neighbours).

I can also change the temperature to change matter from a liquid to a solid.

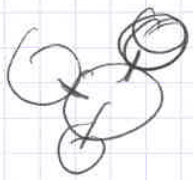
⇒ The jamming transition is a rigidity transition at $T=0$

⇒ occurs at a critical packing fraction ϕ_J; $\phi < \phi_J$ no contact

$\phi = \phi_J$: system is isostatic.

# of degrees of freedom $= DN$ = # of constraints.

# of constraints $= \frac{z}{2} N$

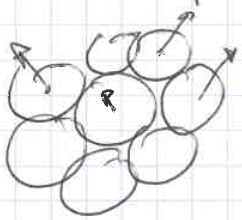


z - # of contacts between particles,

↙ dimension of the system.

$\Rightarrow z_c = 2D$

It also has vibrational properties.



u = displacement vector on every particle

$$u = \begin{bmatrix} u_{1x} \\ u_{1y} \\ \vdots \\ \vdots \end{bmatrix} \Big\} NDx1 \qquad f = \begin{bmatrix} f_{1x} \\ f_{1y} \\ \vdots \\ \vdots \end{bmatrix} \Big\} (NDx1)$$

displacement causes forces.

The linear response

⇒ the dynamical matrix M

For system that have a 2-body potential (see Ashcroft & Mermin):

off-diagonal term

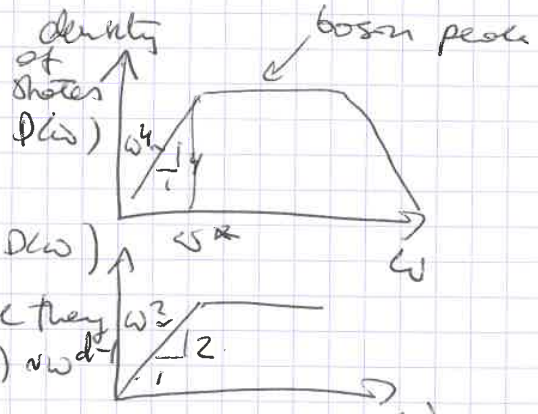
$$M_{i\alpha j\beta} = \frac{\partial^2 V(|r_i - r_j|)}{\partial r_{i\alpha}\, \partial r_{j\beta}}$$

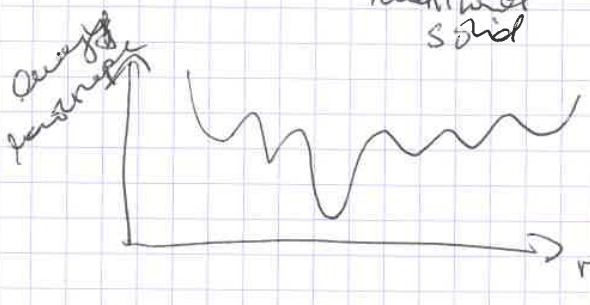
$i\alpha$, $j\beta$: particle index, particle index, direction index

on diagonal terms $M_{i\alpha i\beta} = -\sum_j \frac{\partial V(r_{ij})}{\partial r_{i\alpha}\, \partial r_{j\beta}}$

It looks very much as the random graph Laplacian from Elmi.

Calculate the eigenmodes. eigenvalue $\propto \omega^2$





Thus low frequency modes may be better at fluidizing the system than high frequency ones.

Use Lecture 4

Interacting spp $D_i \to 0$

$$\vec{d}_i = \sum_\nu a_\nu(t)\, \vec{e}_{i,\nu}$$

$\vec{e}_{i,\nu}$: eigenvectors of the dynamical matrix

$$\langle a_\nu(t) \rangle \sim a_\nu(0) + \frac{1}{\omega_\nu^2} C$$

very small t

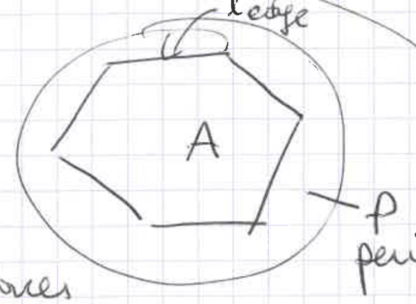
Intermediary III: Vertex models

1. Zero motility limit

$$E_{cell} = \frac{K_A}{2}(A - A_0)^2 + \sum \frac{\Lambda}{2} l_{edge} + \frac{\Gamma P^2}{2}$$

energy bonus if you have a bonder with another cell (cadherins)

$$P = \sum_{edges} l_{edge}$$



What mechanical forces act to regulate cell shapes.

1. Cell - cell adhesion
2. Active cytoskeleton - highly enriched actin-myosin at cell cortex generates cortical tension
3. Fluid filled - many cells don't change their volume easily

cells have a preferred area they like to keep

nonlinear term that is controversial not there in Hufnagel 2007

For a hexagon you can write down the link between Area and perimeter

I assume that all cells have the same pressure.

cadherins:

when they come into contact from two cells

the total energy of all cells is lowered.

It's like a negative surface tension.

Ground states.

$$\bar{\Lambda} = \frac{\Lambda}{K (A_0)^{3/2}}$$

Assume Λ's are the same

$p_0 = \frac{-\Lambda}{\ldots}$

$$E_{tot} = \frac{1}{K_A A_0^2} \sum_i^N E_{cell}^i = \sum_i^N (a_i - 1)^2 + \frac{1}{\Gamma} (p_i - p_0)^2$$

$$\Gamma = \frac{K_A A_0}{K_P}$$ ← ratio area stiffness to perimeter stiffness

$p_0 =$

Homework: Calculate the elastic exponent for Stone EPJE 2010 these values.

Hint: in phase I : $p_i = p_0$ $a_i = 1$ ∀ i

in phase II p_i can relate after a_i

in phase III $p_i = 0$, $a_i = 0$

Beyond ground states

→ you have metastable states (disordered phase)

If I numerically want to study it

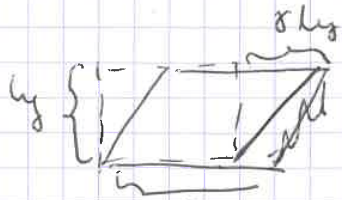
Voronoi tessellation of poisson point process.

optimization from this tessellation

To predict minimization on the vertices given topology for the cryst.

To understand when the system becomes rigid?

~~when~~ we need to know when the shear modulus becomes positive $\mu > 0$.



γ = shear strain

↑ extra Degree of freedom (DOF)

$(N d + 1)$ DOF

shear modulus μ $\mu > 0$

- $E = E(\{r_i\}, \gamma, A)$ ← total energy of the system.
- mechanically stable state at fixed γ.

$$E_{min}(\gamma) = \min_{\{r_i\}} E(\{r_i\}, \gamma, A)$$

(*) $g = \frac{1}{V}\left(\frac{\partial^2 E}{\partial \gamma^2} + \sum_{k,\beta} \frac{\partial^2 E}{\partial r_k^\beta \partial \gamma} \dot{r}_k^{min\,\beta}\right)$ → $\frac{dr_k^{min\,\beta}}{d\gamma}$

define $D_{j\alpha,k\beta} \equiv \frac{\partial^2 E}{\partial r_j^\alpha \partial r_k^\beta} = \sum_m \omega_m^2 u_{j\alpha}^m u_{k\beta}^m$

(vertex; x,y component; eigenvector)

use it to manage g:

$$0 = \frac{\partial E(r_i^{min}(\gamma), \gamma)}{\partial r_j^\alpha}$$ ← force balance eqn. (*)

which happens now:
take total derivative of that eqn (*) with respect to γ:

$$0 = \sum_{k,\beta} D_{j\alpha k\beta} \dot{r}_k^{min,\beta} + \frac{\partial^2}{\partial r_j^\alpha \partial \gamma} \quad (**)$$

$$\bar{D}_{pq} = \frac{\partial^2 E}{\partial z_p \partial z_q}$$

$$z_p = (\vec{r}_1, \vec{r}_2 \ldots \vec{r}_N, \gamma)$$

$$\bar{D}_{pq} = \sum_m \bar{\omega}_m^2 u_p^m \bar{u}_q^m$$ ← If I diagonalize the new extended hessian I'll get different eigenvalues and eigenvectors

$$\dot{\bar{z}}^{min} = (\dot{r}_1^{min} \ldots \dot{r}_{N_v}^{min}, 1)$$

Using (**) in Eq (*)

$$Vg\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ \vdots \\ 1 \end{bmatrix} = \begin{bmatrix} D_{j\alpha,k\beta} & \frac{\partial^2 E}{\partial\gamma\partial r_j} \\ \frac{\partial^2 E}{\partial r_i \partial\gamma} & \frac{\partial^2 E}{\partial\gamma^2} \end{bmatrix} \begin{bmatrix} \dot{r}_1^{min} \\ \vdots \\ \dot{r}_{N_v}^{min} \\ 1 \end{bmatrix}$$

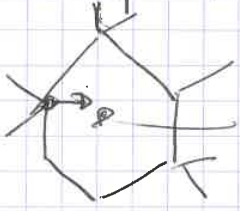
(these E: the $\sum_{k\beta} \frac{\partial^2 E}{\partial r_k^\beta \partial\gamma} \dot{r}_k^{min\beta}$ term $\frac{\partial^2 E}{\partial\gamma^2}$ term from (*) term too)

$$Vg\, \delta_{\gamma p} = \bar{D}_{pq} \dot{\bar{z}}^{min}$$

take scalar product $\bar{u}_p^m$ ↑ / indices of extended hessian (...)

Comment 1:

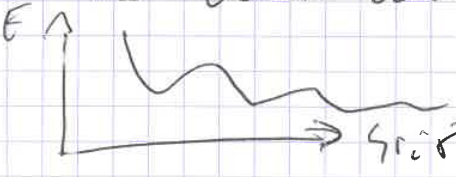
- if there exists a zero mode $\tilde{u}$ with $U_j^{\tilde{u}} \neq 0$ then the shear modulus entry is the j^{th} row of u^m needs to be zero $g=0$ and you get no shear stress.



displacement of the vertex and box

So a zero mode means you displace the whole box so you get no shear stress.

A zero mode means you can use this for trial. What we are doing is adding γ as a degree of freedom and not treating it specially. In general the eigenmodes describe the displacements of the vertices.



put γ as a degree of freedom.

If the shear modulus is larger $g>0$ then the cells can move around.

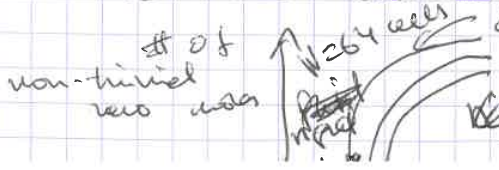
If the shear modulus $g \sim 0$ then the cells can move and:

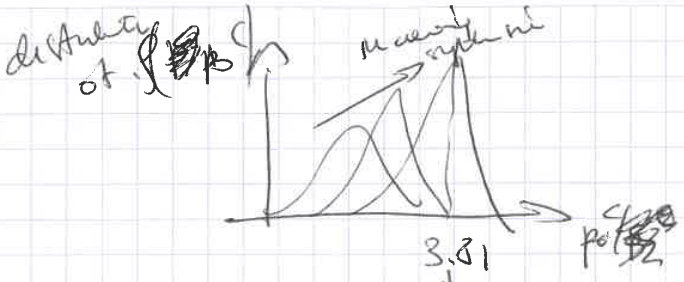
$$g = \frac{1}{V}\left[\sum_{\tilde{m}} \frac{\left(\bar{u}^{\tilde{m}}_{\delta}\right)^2}{\bar{\omega}^{\tilde{m}}}\right]^{-1}$$

$\tilde{m}$: non-trivial zero modes!

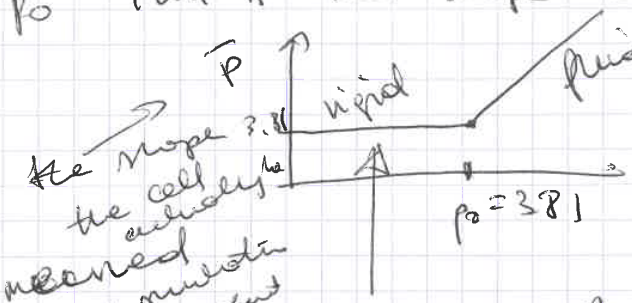
shear modulus is a weighted average of eigenmodes!

You can calculate g as a function of p and prefer this shape of this





thermodynamic transition.

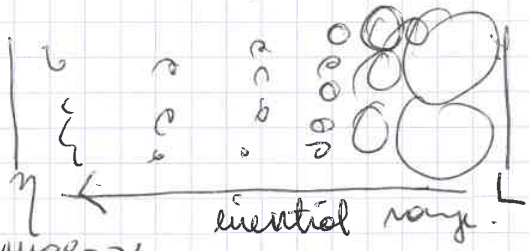


You are stuck, you cannot satisfy the shape you want, & you do not minimize the energy

You are stuck by others around you and the box.

Aquense lecture 4

Turbulence part cont'd:



$$\partial_t \bar{v} + \bar{v}\cdot\bar{\nabla}\bar{v} = \nu\nabla^2\bar{v} - \frac{1}{\rho}\bar{\nabla}p + f$$

(1) $\frac{L}{\eta} \sim Re^{3/4}$

velocity difference

$$v_r = \langle |v(\bar{x}+\bar{r}) - v(\bar{x})| \rangle$$

structure function: $\langle |v(\bar{x}+\bar{r}) - v(\bar{x})|^p \rangle \sim v_r^p = S^p$

correlation function: $\langle |v(\bar{x}+\bar{r})\cdot v(\bar{x})|^p \rangle = C(r)$

$E(k) = 4\pi k^2 \mathcal{F}\langle v(\bar{x}+\bar{r})\cdot v(\bar{x}) \rangle$

$\delta_r v^3 \sim \varepsilon \rightarrow \delta_r^2 V \sim r^{2/3}$ ← here I am skipping the 3rd order and 2nd order moments and scale as well

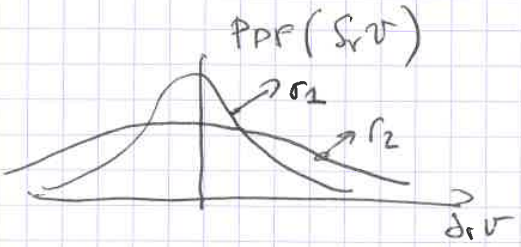
↑ velocity differences

$\Pi = 5/3 \rightarrow E(k) \sim k^{-5/3}$

→ this is self-similarity

self-similarity ⇔ you motivate it by things being scale free at large Reynolds's numbers.

There is no length scale.



The variance of this probability is increasing with the distance $\delta_r^2 v \sim r^{2/3}$

So if $r_2 > r_1$ then at r_2 the distribution is broader.

What about the shape of this distribution? Maybe I can assume it's self-similar (so the rescaled functional form is the same).

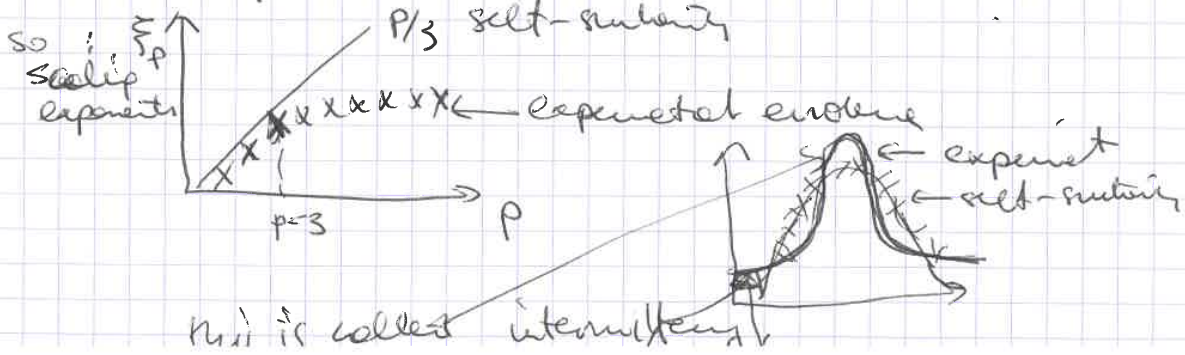
do they rescale? Do they collapse onto each other?

If they do ⇔ all moments will scale.

(1) If yes → all the structure functions will scale.

$S_{2p}(r) \sim S_2(r)^p$ (if $S_2(r) \sim r^{2/3}$)

$\Rightarrow S_{2p}(r) \sim r^{\frac{2}{3}p}$



for a scalar field θ

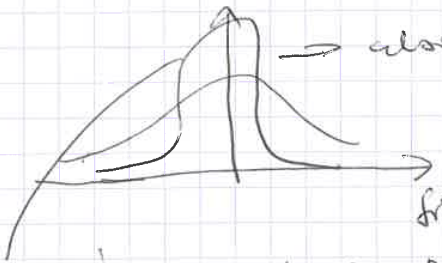
$$\partial_t \theta + \vec{u} \cdot \nabla \theta = D \nabla^2 \theta + f_\theta$$

$\vec{u}$ advecting velocity field; D diffusivity; f_θ

examples of a scalar field → ocean temperature, freezer displays on a fluid

weight that does not effect the fluid velocity

At large Reynolds numbers we would just have diffusion.



the intermittency is even more pronounced than in velocity fields,

→ so you get ramps and cliffs.

The shape of a theoretical ramp and cliff comes from diffusion. Otherwise you would really have ramps & cliffs.

* KRAICHNAN MODEL

scaling exponents $S_2(r) \sim D\, \delta(t-t')$

→ you get zero modes,

why does a scaling argument fail:

$$L(x) = f(x)$$

a solution of a linear problem also contains zero modes. But they are obtained through

$L(x) = 0$ so they will ~~obtain~~ not follow your scaling!

So zero modes are at the origin of

+ Lagrangian framework.

$$\frac{d\theta}{dt} = S(\xi(t), t)$$

↑ source term along the trajectory

$$\frac{d\xi(t)}{dt} = \bar{v}[\xi(t), t] + \eta(t)$$

↑ Eulerian velocity field

the Lagrangian description will follow the trajectory.

So I could write $\frac{d\bar{v}}{dt}$ because it depends on what you look at

so you can recollect the value of your scalar field

$$\theta(\bar{r}, t) = \int dt' \, G(\bar{r}, t \,|\, \bar{r}', t') \, Q(\bar{r}', t')$$

↑ point in space

And if you want to look at two points you need to know how 2-points look next together

And if you look at N points now together

So its a genetic interpretation.

Point sources of scalar field (ODOR)

eventually you only have discrete patches.

at small scales you have gradients and everything is smooth

at large scales there are zeros all over the place

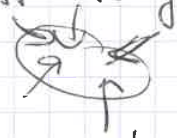
So you move to this second formalism

~ Lagrangian framework.

If you are interested in navigation, how do I find the source of an odor in a fluid environment.

Small scales: Re $\ll 1$ Pe $\ll 1$ for gradients / Large scales ⟶ far away from the source. WIND!

for away from the source gradients are useless because they would point you to the middle.



So you are information limited.

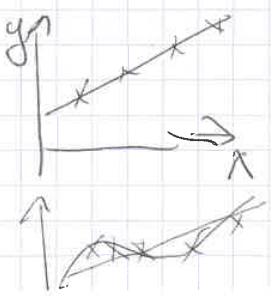
There is a lot of work on how to build an algorithm to find the source.
One is called infotaxis → you climb the information gradient about the source.
The goal is to find the source, not to gain information.
As a function of what information you are after. you will either do well or badly
(two-arm-bandits).

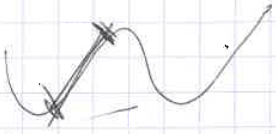
→ nice. fruity notes.

David Schwab lecture 1

What is a machine learning problem?
Why is it difficult and different than what you think?
Most of it will be in such as used in google facebook
But those are open two different things.

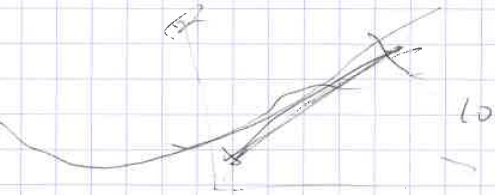
Fitting with no noise



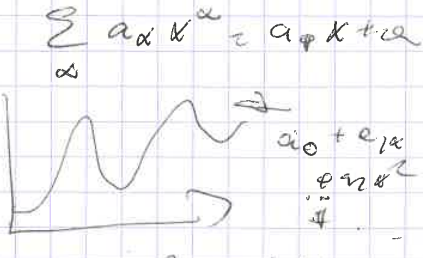


In true reality you are never fitting with the right function and true is noise.

In reality you have noise.



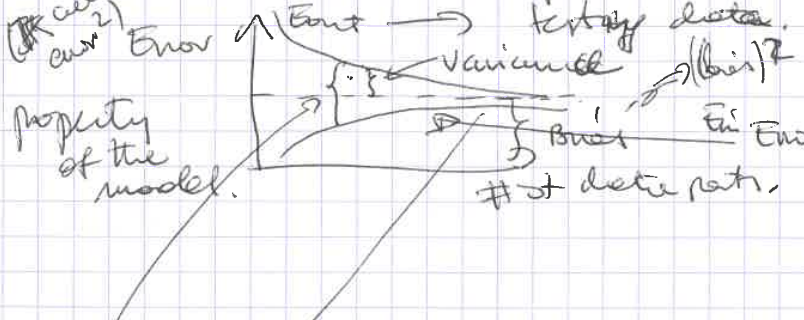
Even if you consider the true function within the range of functions you are considering, the most predictive function may not be the true one (3^{rd} order polynomial is more predictive than the true 10^{th} order polynomial).



More data? To fit 10 parameters? 10000 data points.

Even when it starts behaving right, it may still do something weird outside of the range.

All these examples have the right noise model.



generalization error or generalization gap

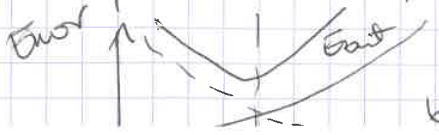
The asymptotic value is called a bias because it's just a property of the model.

in sample = data you have

out sample = testing data.

→ If this is big you are putting better on training data than testing data and it's a signature of overfitting

$\|Test - bias\| \Rightarrow$ Variance → explain more later



for a fixed data size as the model gets more complex it

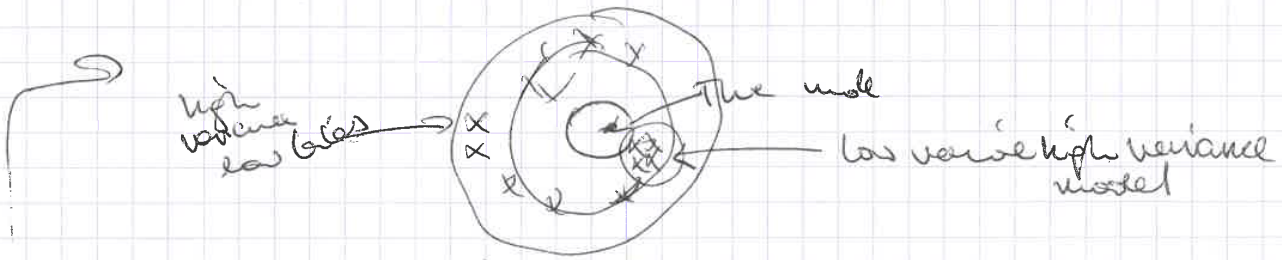
more data as you have more data you do worse because you can't fit all the wiggles for a few data points ideally. Even if it may.

But the variance goes up.

What the variance is: dataset of finite size and I fit to the data set, the parameters depend on this training set.

If I repeat to many data the parameters in parallel universes, I get different parameters and the variance of these parameters increases with model complexity.

So Error is a sum of the variance + bias.



many datasets of fixed size

Switch notation error → cost (same thing)

Dataset $D = \{(\vec{x}, y)\}$

$y = f(\vec{x}) + \varepsilon$

true model is an arbitrary function

noise, zero mean, standard deviation σ_ε

Imagine we have a cost function:

$$C(\{y\}, \{g(\vec{x}; \theta)\}) = \sum_i (y_i - g(\vec{x}_i; \theta))^2$$

model function (that we are fitting)

parameters of the model.

for today: this choice seems reasonable.

But it corresponds to a Gaussian noise model with likelihood (tomorrow more about it).

Find the value of parameters that minimize the

$\hat{\theta}_D = \arg\min_\theta C$

that depends on the data from dataset

how the dataset we are trying to predict

$$\mathbb{E}_{D,\varepsilon}\left[C(y, g(x, \hat{\theta}_D))\right] = \mathbb{E}_{D,\varepsilon}\left[\sum_j (y_j' - g(x_j', \hat{\theta}_D))^2\right]$$

training dataset — testing dataset.

testing datasets

$$= \mathbb{E}_{D,\varepsilon}\left[\sum_j (y_j' - f(x_j) - f(x_j) - g(x_j', \hat{\theta}_D))^2\right] =$$

Rarely break up proper way: train, validation, test but often just two (train, test).

This is like a quenched average: you average over different models ($\hat{\theta}_D$) from different training sets,

$$= \sum_j \mathbb{E}_\varepsilon\left[(y_j' - f(x_j))^2\right] + \mathbb{E}_{D,\varepsilon}\left[(f(x_j) - g(x_j', \hat{\theta}_D))^2\right] +$$

$= \sigma_\varepsilon^2$

same here, no D dependence since f is the true function (g is the one you learn and depends on $\hat{\theta}_D$)

can get rid of testing set average since no y' terms

$$+ 2\,\mathbb{E}_\varepsilon\left[(y_j' - f(x_j))\right]\mathbb{E}_D\left[f(x_j) - g\right]$$

since y_j' is on average equal to the true value (the variances that differ)

$$\mathbb{E}_D\left[(f(x_j) - g(x_j', \hat{\theta}_D))^2\right] = \mathbb{E}_D\left[(f(x_j) - \mathbb{E}_D[g(x_j', \hat{\theta}_D)]\right.$$

$1 = +A - A$

$$= \cancel{\mathbb{E}_D}\Big[\underbrace{\big(f(x_j) - \mathbb{E}_D[g(x_j;\hat{\theta}_D)]\big)^2}_{\text{bias}^2}\Big] +$$

$$+ \mathbb{E}_D\Big[\underbrace{\big(g(x_j;\hat{\theta}_D) - \mathbb{E}_D[g(x_j;\hat{\theta}_D)]\big)^2}_{\text{Variance}}\Big] + \cancel{\text{cross terms}} \; 0$$

because mean is equal to real mean.

does not depend on the data training

how similar is the model we learn every time to the average model you learn

$$\mathbb{E}[\bar{C}(\vec{x})] = \text{noise} + \text{bias}^2 + \text{variance}$$

$\hookrightarrow \sigma_\varepsilon^2$

how different is the true model f from the average model you learn.

blue graph is $C_{in}(\{y_i\}, g(\vec{x}, \theta)) = \frac{1}{N}\sum_i (y_i - g(\vec{x}_i, \theta))^2$

$\Rightarrow$ which gives you $\hat{\theta}_D$

red one is the cost in $\mathbb{E}_{D,\varepsilon}\big[\text{Cost}(y, g(\vec{x}, \hat{\theta}_D))\big]$

So what you care about is running cost and you need to remember about noise, bias^2 + variance.

The exact definition of noise, bias^2 and variance only holds for Gaussian noise models but you get similar definitions for non-quadratic cost functions.