BRANCHING MORPHOGENESIS | BSS '26

EXAMPLES:
- LUNG ALVEOLI, LUNG VASCULATURE
- PLANT ROOT GROWTH
- KIDNEY NEPHRON STRUCTURE
- PURKINJE CELLS (i.e. DENDRITIC NEURONS) in CEREBELLAR CORTEX
- GLANDULAR ARCHITECTURE (e.g. MAMMARY et.)

... SO LET'S TALK ABOUT THE 1D ISING MODEL!

↑ ↑ ↑ ↑ ↓ ↓ ↓ ↑ ↑ ↑ ↑ ↑ ↓ ↓ ↑ ↑

INTERMEDIATE ORDER STATE /DEGENERACY

HOW TO CAPTURE KINETICS?

NOTICE! LOCAL INSTABILITY TO FLIPPING A SPIN AT A DOMAIN BOUNDARY

CONSIDER INSTEAD THE BOUNDARIES, AND LATTICE of "POTENTIAL" BOUNDARIES

↳ LOCAL INSTABILITY AT BOUNDARIES ⇒ RANDOM WALK! (w diff coeff D)

NOW, ARE THERE INTERACTIONS?

① ↑ ↓ ↑ → ← POOF ↑

ANNIHILATION $A + A \to 0$ at rate λ

② ↑ ↓ → N-N SPIN EXCHANGE INSTABILITY ↑ ↓ ↑ ↓

BRANCHING $A \to (m+1)A$ $m \in \mathbb{Z}_{>0}$ at rate σ_m

"BARW MODEL"

MEAN FIELD: $\dot{n}(t) = -2\lambda n(t)^2 + M\sigma_M n(t)$

⇒ MF steady state density $= \frac{M\sigma_M}{2\lambda}$

BUT THIS IS WRONG FOR KINETIC ISING DUE TO FLUCTUATIONS!

↳ $d_{uc} = 2$, $d_{LL} = 4/3$

c.f. JARDY & TAUBER 1996

IN DETAIL, M odd vs M even differ (i.e. different universality class) due to parity conservation symmetry

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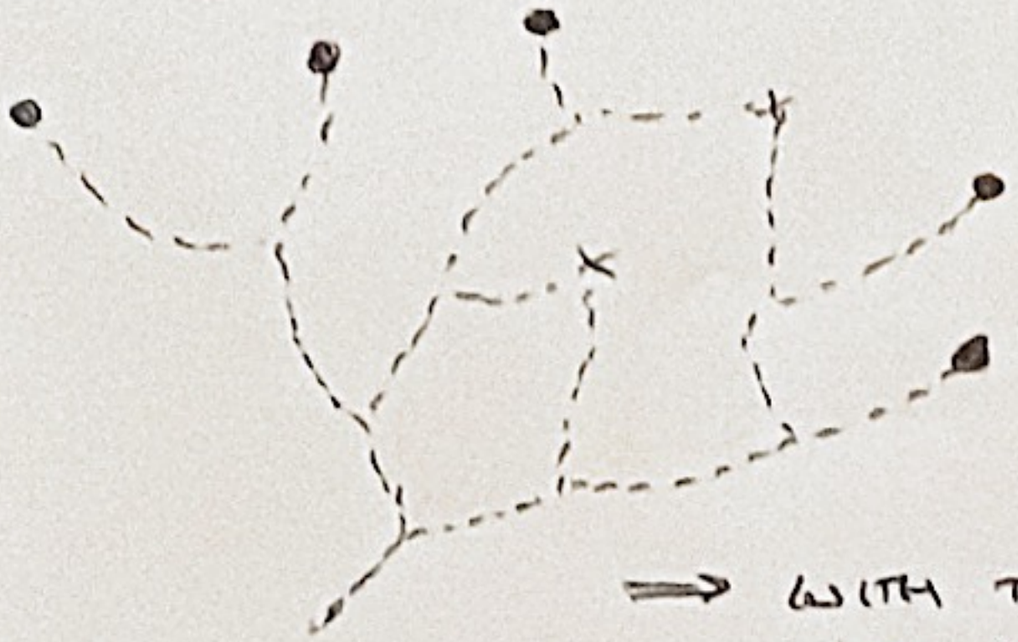
BUT! ABOVE THE UPPER CRITICAL DIMENSION THIS NO LONGER MATTERS

EXAMPLE: CONSIDER $d = 3$, $M = 1$



POINTS DIFFUSING AROUND IN SPACE, RANDOMLY SPLITTING INTO TWO, & ANNIHILATING IF THEY COME TOO CLOSE TOGETHER

$\Longrightarrow$ WITH TRAJECTORIES INCLUDED THIS LOOKS A LOT LIKE BRANCHING MORPHOGENESIS!

... WHAT WERE WE TALKING ABOUT AGAIN? BACK TO BRANCHING MORPHOGENESIS!

BARW ALONE NOT ENOUGH $\rightarrow$ NEED TO CAPTURE THE PAST TRAJECTORIES

2-STATE EXTENSION OF BARW MODEL: A, I

A diffuses in d-dimil (eg. 3d) spac w/ coeff D_A

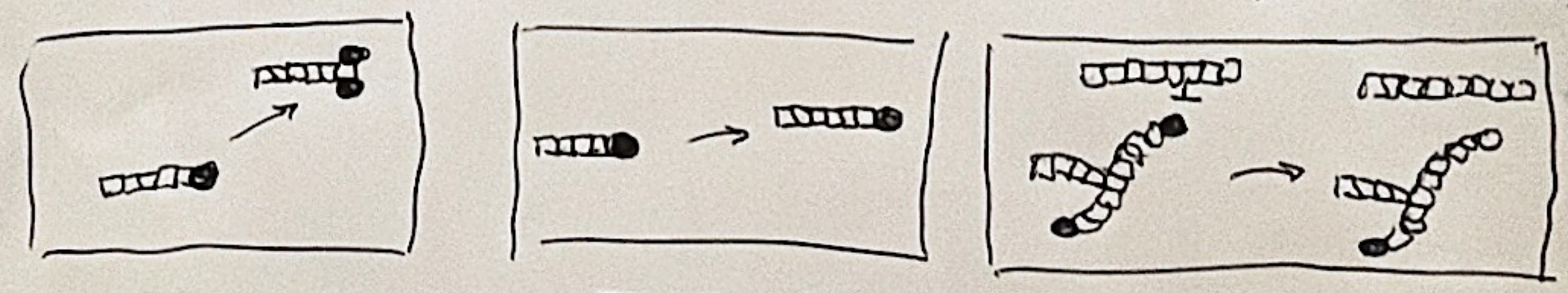
I stationary

$A \rightarrow I + A$ (A lays down I as it goes)

$A \rightarrow (M+1)A$ (A can branch into M+1 As)

$A + A \rightarrow I + I$ (two As coming close together annihilate into Is)

(&c) $A + \tilde{I} \rightarrow I + \tilde{I}$ (A coming close to a "non-local" I, annihilates into I)



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MEAN FIELD DYNAMICS (w/o (*) first...) $d=3$, $\mu=1$

$$\dot{a} = D\nabla^2 a + \sigma_1 a\left(1 - \frac{a}{a_0}\right) \leftarrow \text{Fisher-KPP!}$$

$$\dot{i} = r_e a + \frac{r_b}{a_0} a^2 \leftarrow \text{purely slaved to } a$$

for a_0 a saturation concentration where branching and annihilation balance

$\Rightarrow$ Fisher Wave front invasion of growing tips

front w/ characteristic length $\sqrt{D/\sigma_1}$

solitary wave velocity $\sim \sqrt{D\sigma_1}$

But! w/o the INTERACTION $\mathcal{H}$ $A \neq I$ the active tips remain active infinitely far behind the front forever

$\Rightarrow$ INCLUDING (*) BREAKS MARKOVIAN NATURE OF THE PROBLEM AND UNDOES THE SLAVING of $I \mapsto A$:

$$\dot{a} = D\nabla^2 a + \sigma_1 a\left(1 - \frac{a+i}{n_0}\right)$$

$$\dot{i} = r_e a + \frac{\sigma_1}{n_0} a(a+i)$$

IN GENERAL, NON-INTEGRABLE EQS,

taking physiological limits $a \ll i$ and $\frac{\sigma_1}{r_e}(a+i) \ll 1$

gives Fisher-KPP PULSES WHICH ARE

OBSERVED IN EXPERIMENTS!

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NETWORK ADAPTATION DYNAMICS & CYCLE STABILIZATION

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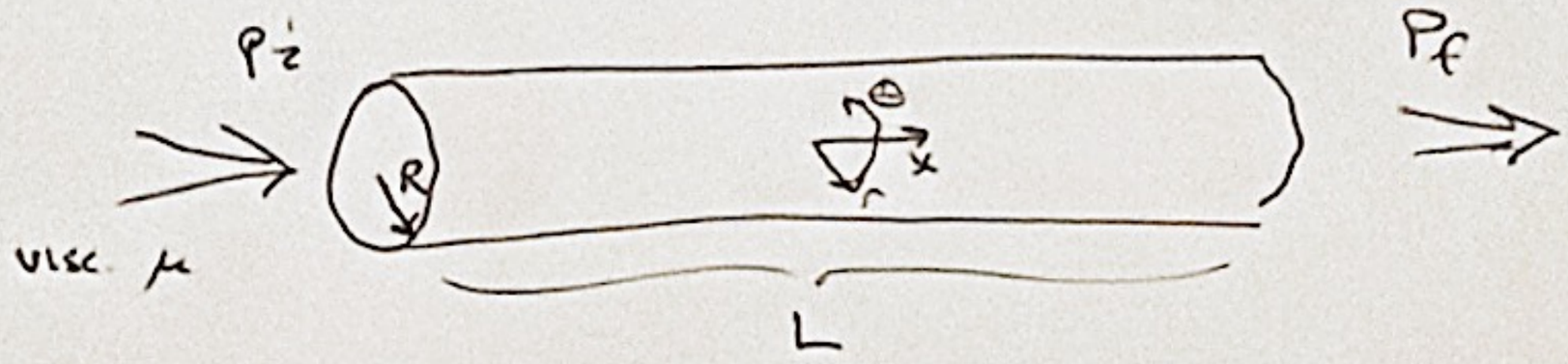
(LAMINAR) FLOW IN A TUBE



START: Navier-Stokes momentum eqs. (in 3d cylindrical coords)

ASSUME: ① STEADY FLOW $\Rightarrow \frac{\partial}{\partial t}[\,] = 0$

② (ONLY) AXIAL FLOW $\Rightarrow u_r = u_\theta = 0$

③ AXISYMMETRIC FLOW $\Rightarrow \frac{\partial}{\partial \theta}[\,] = 0$

④ FULLY DEVELOPED FLOW $\Rightarrow \frac{\partial u_x}{\partial x} = 0$ given ①-②-③ equiv. to mass conservation

THEN:

- ANGULAR MOMENTUM EQ: $0 = 0$
- RADIAL MOMENTUM EQ: $\frac{\partial p}{\partial r} = 0$
- AXIAL MOMENTUM EQ: $\underbrace{\frac{1}{r}\frac{\partial}{\partial r}\left(r\,\frac{\partial u_x}{\partial r}\right)}_{f(r)} = \underbrace{\frac{1}{\mu}\frac{\partial p}{\partial x}}_{g(x)}$ $\Rightarrow$ each side is (same) constant

$$\Rightarrow -\frac{dp}{dx} = \frac{\Delta p}{L}$$

$$\Rightarrow u_x = \frac{\Delta p\, r^2}{4L\mu} + C_1 \ln r + C_2$$

$C_1 = 0$, need u_x finite at $r = 0$

$\leftarrow$ no-slip boundary condition $\Rightarrow C_2 = \frac{\Delta p R^2}{4L\mu}$

$\Rightarrow$ PARABOLIC VELOCITY PROFILE $u_x = \frac{\Delta p}{4\mu}(R^2 - r^2)$

$$u_{max} = u_x(r=0) = \frac{\Delta p R^2}{4L\mu} \;;\; u_{avg} = \frac{1}{\pi R^2}\int_0^R 2\pi r\, u\, dr = \frac{1}{2}u_{max}$$

EXP. ACCESSIBLE: VOLUMETRIC FLOW RATE $Q = \pi R^2 u_{avg}$

$$\Rightarrow Q = \pi R^2 \frac{\Delta p R^2}{8L\mu} \rightsquigarrow \boxed{\Delta p = \frac{8\mu L}{\pi R^4} Q}$$

Hagen-Poiseuille

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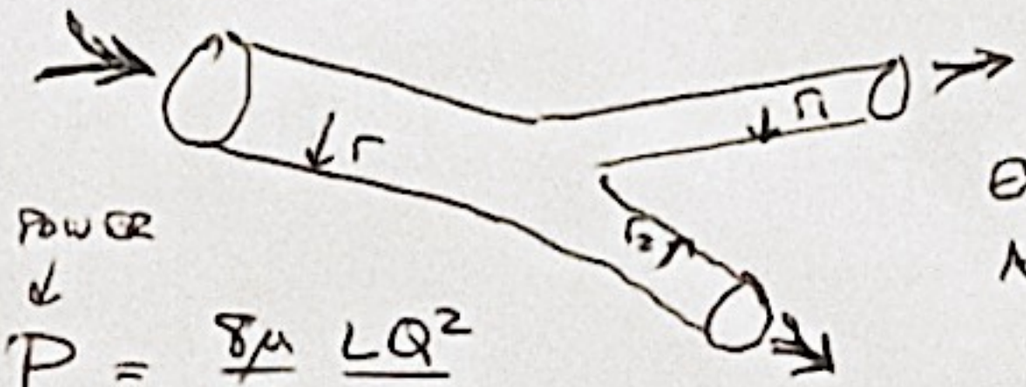
WHAT ABOUT JUNCTIONS?



IS THERE AN EXPECTED RELATIONSHIP AMONG r, r_1, r_2 ?

HAGEN-POISEUILLE

$$Q = \frac{\pi}{8\mu}\frac{R^4}{L}\Delta p \Rightarrow P = \frac{8\mu}{\pi}\frac{LQ^2}{R^4}$$

(P: POWER)

MINIMIZE POWER CONSUMPTION : R (i.e. r, r_1, r_2) $\to \infty$ NEED A BALANCING COST

→ ASSUME POWER DENSITY FOR MAINTAINING PIPE IS λ

↳ PIPE HAS $V = \pi R^2 L$

⇒ TOTAL POWER CONSUMPTION $\sum_{\text{PIPES}} (P_f + P_M) \overset{\text{single flow}}{=} \frac{8\mu}{\pi}\frac{LQ^2}{R^4} + \pi\lambda L R^2$

MINIMIZE POWER CONSUMPTION NOW?

EXACT MINIMIZATION DOWN TO DETAILS OF WHAT CAN BE MANIPULATED, IN GENERAL THE TERMS SHOULD BE PROPORTIONAL:

$\Rightarrow Q \propto R^3$

ASSUME LEAKLESS FLOW & MASS CONSERVATION AT THE JUNCTION:

$$\sum_{\text{in}} Q_i = \sum_{\text{out}} Q_j \Rightarrow \boxed{r^3 = r_1^3 + r_2^3}$$

"MURRAY'S LAW"

OTHER POSSIBILITIES:

PASSIVE DIFFUSIVE TRANSPORT

$$r^2 = r_1^2 + r_2^2$$

TURBULENT FLOW

$$r^{7/3} = r_1^{7/3} + r_2^{7/3}$$

ASIDE: SIMPLEST MINIMIZATION (ONLY R MANIPULABLE)

$$\frac{\partial P}{\partial R} = \frac{8\mu L Q^2}{\pi}(-4)\frac{1}{R^5} + 2\pi\lambda L R$$

$$0 = -\frac{16\mu Q^2}{\pi}\frac{1}{\tilde{R}^5} + \pi\lambda\tilde{R}$$

$\tilde{R}$: POWER MINIMIZING R

$$Q^2 = \frac{\pi^2\lambda}{16\mu}\tilde{R}^6$$

$\Rightarrow Q \propto \tilde{R}^3$ ✓

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MURRAY GIVES AN OPTIMAL RELATIONSHIP FOR A SINGLE JUNCTION, JOIN TOGETHER FOR A NETWORK? DYNAMICS?

BIOLOGY EXAMPLES: POLYCEPHALUM PHYSARUM (cf "LEARNING")
VASCULATURE (LUNG, MUSCLE) - TREES
VASCULATURE (ALL OTHER ORGANS) - CYCLIC
LEAF VENATION - USUALLY CYCLIC
RIVERS (IN THE WATERSHED) - TREES
RIVERS (IN THE DELTA) - CYCLIC
PANCREAS DUCTAL NETWORK

LET'S REWRITE THE POWER CONSUMPTION IN TERMS OF $C_i = \frac{\pi}{8\mu}\frac{R_i^4}{L_i}$ (CONDUCTANCE):

$$P_i = \left(\frac{Q_i^2}{\tilde{C}_i^2} + C_0 \tilde{C}_i^{\gamma}\right) L_i \qquad \tilde{C}_i = C_i L_i$$

generalize maintenance cost; $\gamma = \frac{1}{2}$ for blood vessels

$\Rightarrow$ LET'S ASSUME WE HAVE ONE SOURCE NODE, ALL OTHERS ARE SINKS AND AN INITIAL LATTICE w/ C_0 EVERYWHERE

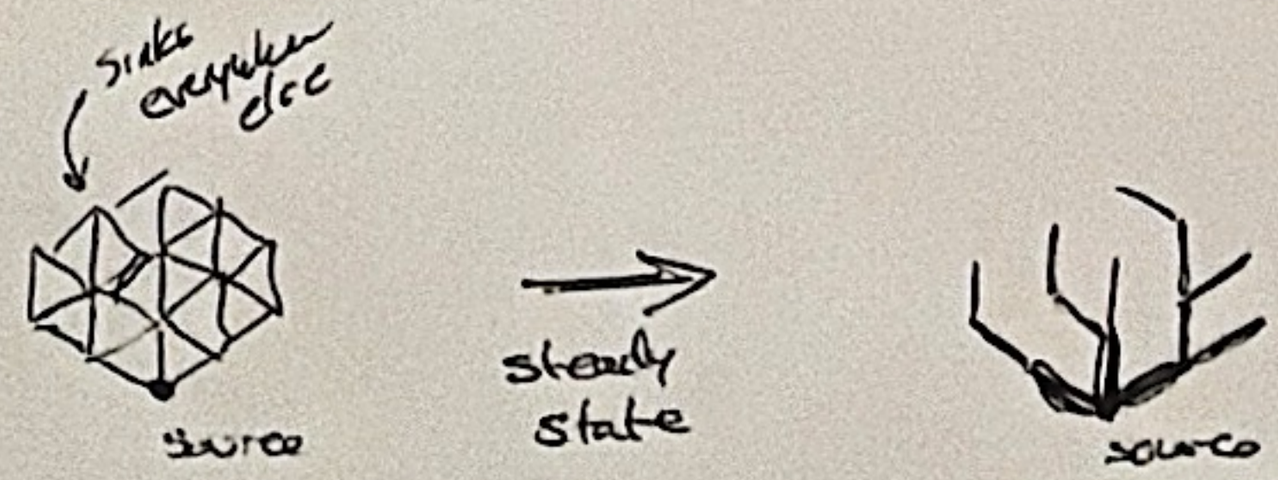
CONSIDER THE FOLLOWING DYNAMICS:

$$\frac{d\tilde{C}_i}{dt} = c\left(\frac{Q_i^2}{\tilde{C}_i^{\gamma+1}} - \tilde{\tau}_e^2\right)\tilde{C}_i$$

wall shear stress squared $= \tau_i^2$; optimal wall shear stress squared

NOTE:
① GLOBAL COUPLING!
② $\tau_i < \tau_e \Rightarrow \frac{d\hat{C}_i}{dt} < 0$
CAN EXPONENTIALLY DRIVE $\hat{C}_i \to 0$

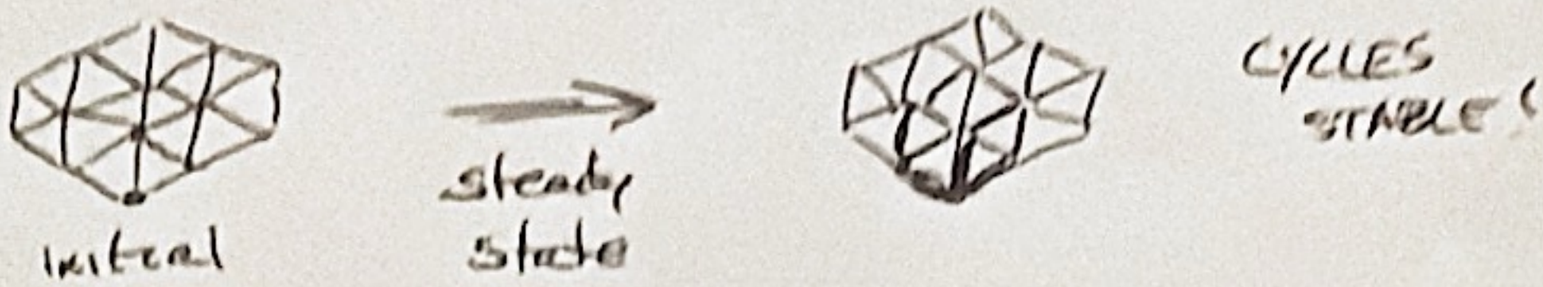
$\tau_i > \tau_e$ TOO MUCH FLOW FOR THE CONDUCTANCE!
$\frac{d\hat{C}_i}{dt} > 0$



CAN WE MODIFY THE DYNAMICS TO STABILIZE CYCLES?

WHAT IF ADAPTATION IS SLOW COMPARED TO FLUCTUATING SINK DEMANDS?

$$\frac{d\tilde{C}_i}{dt} = c\left(\frac{\langle Q_i' \rangle}{\tilde{C}_i^{\alpha+1}} - \tilde{\pi}_c^*\right)\tilde{C}_i$$



HOW MANY CYCLES ARE THERE?

$\Rightarrow$ CYCLE SPACE (VECTOR SPACE OVER $\mathbb{Z}_2$)

$\cong H_1(G)$

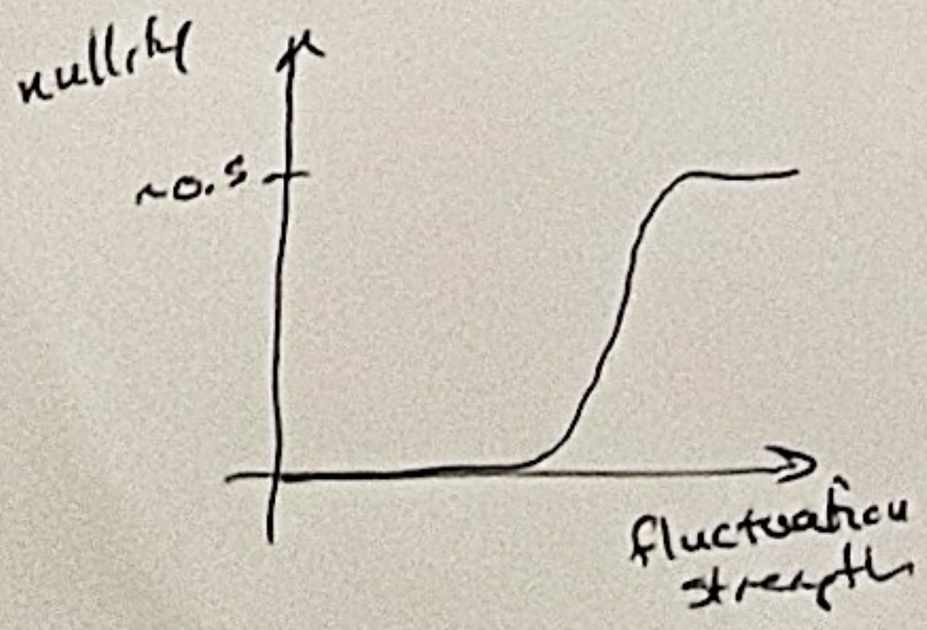
$\dim(H_1(G))$ = # linear indep cycles

define Nullity: $\equiv \dfrac{\dim(H_1(G_k))}{\dim(H_1(G_i))}$

Can we calculate $\dim(H_1(G))$ easily?

CONSIDER a spanning tree, T of G and let $\tilde{e}_i$ be an edge not in T then $T \cup \tilde{e}_i$ has exactly one cycle and $T \cup \tilde{e}_i$ and $T \cup \tilde{e}_j$ are linearly indep

$\Rightarrow \dim(H_1(G)) = e - V + 1$



ALSO!

Cycles can be stabilized with • (non-physical) choices of δ

- spatial coupling b/t two (3d) networks
- metabolic effects / signalling

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NAVIER-STOKES MOMENTUM EQS, 3D CYLINDRICAL COORDS (GRAVITY-FREE)

$$r: \rho\left(\partial_t u_r + u_r \partial_r u_r + \frac{u_\theta}{r}\partial_\theta u_r + u_x \partial_x u_r - \frac{u_\theta^2}{r}\right)$$

$$= -\partial_r p + \mu\left(\frac{1}{r}\partial_r(r\partial_r u_r) + \frac{1}{r^2}\partial_\theta^2 u_r + \partial_x^2 u_r - \frac{u_r}{r^2} - \frac{2}{r^2}\partial_\theta u_\theta\right)$$

$$+ \frac{1}{3}\mu\partial_r\left(\frac{1}{r}\partial_r(r u_r) + \frac{1}{r}\partial_\theta u_\theta + \partial_x u_x\right)$$

$$\theta: \rho\left(\partial_t u_\theta + u_r \partial_r u_\theta + \frac{u_\theta}{r}\partial_\theta u_\theta + u_x \partial_x u_\theta + \frac{u_r u_\theta}{r}\right)$$

$$= -\frac{1}{r}\partial_\theta p + \mu\left(\frac{1}{r}\partial_r(r\partial_r u_\theta) + \frac{1}{r^2}\partial_\theta^2 u_\theta + \partial_x^2 u_\theta - \frac{u_\theta}{r^2} + \frac{2}{r^2}\partial_\theta u_r\right)$$

$$+ \frac{1}{3}\mu\frac{1}{r}\partial_\theta\left(\frac{1}{r}\partial_r(r u_r) + \frac{1}{r}\partial_\theta u_\theta + \partial_x u_x\right)$$

$$x: \rho\left(\partial_t u_x + u_r \partial_r u_x + \frac{u_\theta}{r}\partial_\theta u_x + u_x \partial_x u_x\right)$$

$$= -\partial_x p + \mu\left(\frac{1}{r}\partial_r(r\partial_r u_x) + \frac{1}{r^2}\partial_\theta^2 u_x + \partial_x^2 u_x\right)$$

$$+ \frac{1}{3}\mu\partial_x\left(\frac{1}{r}\partial_r(r u_r) + \frac{1}{r}\partial_\theta u_\theta + \partial_x u_x\right)$$

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