Living flows

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Acknowledgements

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Marcelo Magnasco (Rockefeller)
Kaare Jensen (TU Denmark)
Douglas Daly (Bronx Bot Gardens)
Patrick Drew (Penn State)
Webs surround us
Plant vascular network: The xylem

Water column under tension.
Dangers of cavitation and embolisms
Photosynthetic efficiency is limited by water potential at the leaf.
“What should a biological theory look like”

... 

... 

“Understand the emergence of functional phenotypes
At multiple scales and in multiple systems
Gene -> cell -> organism -> environmental adaptation”

...
Optimal living webs
Evolution

First leaves: no loops!
Adiantites (330 myo)

First plants: dichotomously branching

First simple anastomosing patterns
Glossopterys

Gingko (200 myo)

Barthelopteris (250 myo)

Images from *Paleobotany*, Taylor, Taylor and Klings
**Evolution**

Barthelopteris (250 myo)

Evolution of hierarchical structures

Modern angiosperms (140 myo)

Convergent evolution:
Ferns independently evolved reticulate vascular structures

Wang and Zhang (2009)

Hausmania (200 myo)
Many ways to confer robustness
Many ways to confer robustness
Many ways to confer robustness
Many ways to confer robustness
Optimization

What is the best way to organize the network?

The equations that govern the flow are equivalent to the equations of a resistor network

Kirchhoff: \( V = I R \)

Fix the source (net) currents

Fix the cost to build network

Minimize average water pressure drop
Optimization

Zooming in

Ronellenfitsch, phd thesis 2016
EK, Comptes Rendus Physique 2018
Optimization

Zooming in even more
The phloem
(A) Picea omorika
Abies nordmanniana
Pinus cembra
Pinus palustris

10 cm

(B) Picea omorika Abies nordmanniana Pinus cembra Pinus palustris

100 μm

(a) total sieve element area (10^4 μm²)

distance from tip (mm)
\[ J(x) = Q(x)c(x) \quad \text{sugar current} \]

\[ \frac{dj}{dx} = \Gamma, \quad \text{conservation of sugar mass} \]

\[ \frac{dQ}{dx} = 2 \frac{L_p A}{r_0} (RT \Delta c - \Delta p) \quad \text{water enters by osmosis} \]

\[ u = \frac{Q}{A} \quad \text{flow speed} \]

\[ J = uAc = \Gamma x \]

\[ W = Q(L)\Delta p = \frac{\mu \Gamma^2}{k c_0^2} \int_0^L dx \frac{x}{A(x)} \]

\[ u(x) = -\frac{k}{\mu} \frac{d\rho}{dx} \quad \text{Darcy's law} \]

\[ \frac{d\rho}{dx} = -\frac{\mu \Gamma x}{k c(x) A(x)} \]

\[ dW = -(Q \, d\rho + p \, dQ) \quad \text{dissipation} \]

\[ V_0 = \int_0^L A(x) \, dx \quad \text{total volume} \]

\[ N(x) = \frac{A(x)}{A_0} = \frac{3}{2} \langle N \rangle \left( \frac{x}{L} \right)^{1/2} \]
Building the living webs
Flow regulates arterial-venous differentiation in the chick embryo yolk sac

Fig. 1. Overview of arterial-venous differentiation in the yolk sac. (A) Yolk sac vessels just after the onset of perfusion. The vitelline artery (VA) is just beginning to form. Direction of arterial and venous blood flow is indicated by red and blue arrows respectively. The heart is indicated (*). (B) Schematic representation of vascular system as seen in the boxed area in A. Arteries (red arrows) carry blood away from the heart and veins (blue arrows) carry blood back toward the heart. Note that arteries and veins are in a cis-cis configuration. (C) Embryo 26 hours later than in A. (D) Schematic representation of the vascular system as seen in the boxed area in C. Veins are drawn in white, the direction of venous flow is shown by blue arrows. Arteries are drawn in black, arterial flow is indicated by the red arrows. Note that veins have come to lie parallel to arteries, a venous network is covering the arterial network dorsally. SV, sinus vein. Scale bar: 1100 μm.

Noble et al, Development 2003
“Blood vessels widen with flow”

Richard Thoma (1847-1923)

Untersuchungen über die Histogenese und Histomechanik des Gefässsytems (1893)
How does nature build a (very) efficient transport network?

adaptation equation

\[ \frac{dC_e}{dt} = a|I_e|^{2\sigma} - bC_e \]

local information!

conductivity

flow

Physarum


Arteries/veins

Vascular remodelling

Richard Thoma (1893)
How does nature build a (very) efficient transport network?

adaptation equation

$$\frac{dC_e}{dt} = a|I_e|^{2\sigma} - bC_e + g$$

local information!

conductivity

flow

Physarum


Arteries/veins

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adaptation equation

$$\frac{dC_e}{dt} = a|I_e|^{2\sigma} - bC_e + g$$

local information!

Leaves

Physarum

Arteries/veins
Vascular remodelling
Richard Thoma (1893)
The model

\[ \frac{dC_{ij}}{dt} = a(I_{ij})^2 \gamma - bC_{ij} + g \]

adaptation equation
local information!

Global hydrodynamic coupling

\[ I_{ij} = C_{ij}(p_i - p_j) \]

\[ \sum_j I_{ij} = s_j \]

\[ \hat{\mathbf{L}} \mathbf{p} = \mathbf{s} \quad \text{Poisson equation} \]
The model

\[ \frac{dC_{ij}}{dt} = a(I_{ij})^2 + bC_{ij} + g \]

adaptation equation
local information!

Global hydrodynamic coupling

\[ I_{ij} = C_{ij}(p_i - p_j) \]
\[ \sum_j I_{ij} = s_j \]

\[ \hat{L}\vec{p} = \vec{s} \] Poisson equation

\[ \vec{s}(t) = \vec{s}_0 e^{t/\tau} \] Growth
\[
\frac{dC_{ij}}{dt} = a(I_{ij})^2 \gamma - bC_{ij} + \mathcal{G}
\]

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

\[
E = \sum_i \left(\frac{Q_i^2}{\bar{C}_i} + c_0 \bar{C}_i^{\gamma}\right)L_i
\]

\[
\frac{d\tilde{C}_i}{dt} = c'\left(\frac{\langle Q_i^2 \rangle}{\bar{C}_i^{\gamma+1}} - \bar{\tau}_e^2\right)\tilde{C}_i
\]

\[
\langle Q_i^2 \rangle = (1 - p)\sum_k Q_{i,k}^2 + p\bar{Q}_i^2.
\]

Hu and Cai, PRL 2013
Extracting the salient parameters

\[ F = KL^{-1} \Delta p, \quad F_e = K_e (p_j - p_i) / L_e \]
\[ \Delta^T F = S \]
\[ F = KL^{-1} (\Delta^T KL^{-1} \Delta)^T S \]

Scaling of growth

\[ p = \lambda_t^2 p' \]
\[ L = \lambda_t L' \]
\[ K = \lambda_t^{2\gamma \delta} K' \] (will be deduced later)
\[ S = \lambda_t^\delta S' \] (depends on geometry of fed region. \( = 2 \) for retina)
\[ F = \lambda_t^\delta F' \]

\[ \frac{dK_e}{dt} = a \left( \frac{F_e}{\hat{F}} \right)^{2\gamma} - bK_e + c. \]
\[ \lambda_t = \exp \left( \frac{r}{2} t \right) \]
\[ \frac{dK_e'}{dt} = a \left( \frac{F_e'}{\hat{F}'} \right)^{2\gamma} - b'K_e' + \lambda_t^{-2\gamma \delta} c. \]
\[ b' = (b + r \gamma \delta) \]
\[ \frac{d\hat{K}_e}{d\tilde{t}} = \hat{F}_e^{2\gamma} - \hat{K}_e + \kappa \exp \left( -\tilde{t} / (1 + \rho) \right). \]
\[ \kappa = (c/a) (\hat{F}^\gamma / \hat{S}^\gamma), \quad \text{growth strength} \]
\[ \rho = b / (r \gamma \delta), \quad \text{growth timescale} \]
\[ E = \sum_e L'_e \left( \frac{F'_e}{K'_e} \right)^2 = \sum_e L'_e (K'_e)^{\frac{1}{\gamma} - 1} = \text{const} \]

What I will say is only applicable in the initial stages of growth.

Extracting the salient parameters

\[ F = KL^{-1} \Delta p, \quad F_e = K_e(p_j - p_i)/L_c \]

\[ \Delta^T F = S \]

\[ F = KL^{-1} \Delta (\Delta^T KL^{-1} \Delta)^t S \]

scaling of growth

\[ p = \lambda_t^\delta p' \]

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\[ S = \lambda_t^\delta S' \] depends on geometry of fed region. =2 for retina

\[ F = \lambda_t^\delta F' \]

\[ \frac{dK_e}{dt} = a \left( \frac{F_e}{\hat{F}} \right)^{2\gamma} - bK_e + c. \]

\[ \lambda_t = e^{\frac{r^\delta}{2} t} \]

\[ \frac{dK_e'}{dt} = a \left( \frac{F_e'}{\hat{F}'} \right)^{2\gamma} - b'K_e' + \lambda_t^{-2\gamma \delta} c. \]

\[ b' = (b + r\gamma \delta) \]

\[ \frac{d\tilde{K}_e}{d\tilde{t}} = \tilde{F}_e^{2\gamma} - \tilde{K}_e + \kappa \exp\left(-\tilde{t}/(1 + \rho)\right) \]

\[ \kappa = (c/a) \left( \frac{\hat{F}}{\hat{S}} \right)^{2\gamma}, \] growth strength

\[ \rho = b/(r\gamma \delta) \] growth timescale

\[ E = \sum_e L_e \left( \frac{F_e'}{K_e'} \right)^2 \]

\[ \sum_e L_e' \left( K_e' \right)^{\frac{1}{\gamma} - 1} \equiv \text{const} \]

Dynamics of growth

Ronellenfitch, EK PRL (2016)
Growth: It makes you more efficient!

Local adaptation rules lead to global optimum when growth is present.

Growth period is too short: growth is weak compared to adaptation.

Growth period is long: growth is initially strong compared to adaptation.

Dissipation of "global" optimum as found by annealing.

Ronellenfitch, EK PRL (2016)
Growth: It makes you more developmentally robust!

The model

Fluctuations

\[ \Sigma_j I_{ij}^\nu = s_j^\nu \]
\[ I_{ij}^\nu = C_{ij} (p_i - p_j) \]
\[ \hat{L} \vec{p}^\nu = \vec{s}^\nu \]

\[ \frac{dC_{ij}}{dt} = a \langle I_{ij}^2 \rangle^\nu - bC_{ij} + g \]

\[ S_i^{(j)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
The model

Fluctuations

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\[ \frac{dC_{ij}}{dt} = a \langle I_{ij}^2 \rangle^{\nu} - b C_{ij} + g \]

\[ S_{(j)}^{(i)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
The model

Fluctuations

\[ \sum_j I_{ij}^\nu = s_j^\nu \]

\[ I_{ij}^\nu = C_{ij}(p_i - p_j) \]

\[ \hat{L}\vec{p}^\nu = \vec{s}^\nu \]

\[ \frac{dC_{ij}}{dt} = a\langle I_{ij}^2 \rangle^\nu - bC_{ij} + g \]

\[ S_i^{(j)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
The model

Fluctuations

\[ \Sigma_j I_{ij}^\gamma = s_j^\gamma \]

\[ I_{ij}^\gamma = C_{ij} (p_i - p_j) \]

\[ \hat{L}\vec{p}^\gamma = \vec{s}^\gamma \]

\[ \frac{dC_{ij}}{dt} = a \langle I_{ij}^2 \rangle^\gamma - bC_{ij} + g \]

\[ S_i^{(j)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
The model

Fluctuations

\[ \Sigma_j I_{ij}^v = s_j^v \]
\[ I_{ij}^v = C_{ij} (p_i - p_j) \]
\[ \hat{Lp}^v = \hat{s}^v \]

\[ \frac{dC_{ij}}{dt} = a \langle I_{ij}^2 \rangle^v - bC_{ij} + g \]

\[ S_{(i)}^{(j)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
The model

Fluctuations

\[ \Sigma_j I_{ij}^v = s_j^v \]
\[ I_{ij}^v = C_{ij}(p_i - p_j) \]
\[ \hat{L}\vec{p}^v = \vec{s}^v \]

\[ \frac{dC_{ij}}{dt} = a\langle I_{ij}^2 \rangle^v - bC_{ij} + g \]

\[ S_i^{(j)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
The model

Fluctuations

\[ \Sigma_j I_{ij}^\vee = s_j^\vee \]

\[ I_{ij}^\vee = C_{ij} (p_i - p_j) \]

\[ \hat{L} \vec{p}^\vee = \vec{s}^\vee \]

\[ \frac{dC_{ij}}{dt} = a\langle I_{ij}^2 \rangle^\vee - bC_{ij} + g \]

\[ S_i^{(j)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
The model

Fluctuations

\[ \sum_j I_{ij}^\nu = s_j^\nu \]

\[ I_{ij}^\nu = C_{ij} (p_i - p_j) \]

\[ \hat{L} p^\nu = \tilde{s}^\nu \]

\[ \frac{dC_{ij}}{dt} = a \langle I_{ij}^2 \rangle^\nu - bC_{ij} + g \]

\[ S_i^{(ij)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]
Adding fluctuations in the load during development introduces loops

\[ S_i^{(j)} \propto c + e^{-\frac{d_{ij}}{2\sigma^2}} \]

\[ \frac{dC_{ij}}{dt} = a\langle I_{ij}^2 \rangle^\nu - bC_{ij} + g \]

H. Ronellenfitsch, EK (submitted)
The economics of phenotypic space

Optimally balancing competing objectives

\[ C = \sum_{e} L_e K_e \]
The economics of phenotypic space

Optimally balancing competing objectives

\[ C = \sum_e L_e K_e \]

\[ \hat{A} = \sum_e \frac{A_e}{A_{\text{tot}}} \]

percolation penalty
Pareto front

\[
\hat{A} = \sum_e \frac{A_e}{A_{\text{tot}}} \\
E = \sum_e L_e \frac{F_e^2}{K_e} \\
C = \sum_e L_e K_e^\gamma
\]

percolation penalty dissipation cost

2d embedding of the Pareto front using multidimensional scaling. The geometry of the Pareto front is a one-dimensional line, parametrized by \( \sigma \).

EK, H. Ronellenfitsch, (σθβμιττεδ)
**Tree archetype**

- **Low cost**
  - high percolation penalty
  - hierarchical

- **Increasing fluctuation intensity**

- **“chickenwire” archetype**
  - high cost
  - low percolation penalty
  - uniform

H. Ronellenfitsch, EK (submitted)
There is (much) more to the story!

Leaf fingerprinting

Architectures that are similarly “loopy” can have different structure

σ vein density
a mean distance between veins
A mean areole area
ρ areole density
d average vein diameter weighted by length of venation between junctions

There is (much) more to the story!
Something is missing!

adaptation equation

$$\frac{dC_e}{dt} = a|I_e|^{2\sigma} - bC_e + g + ?$$

Tissue can be hyperperfused near the source but hypoxic near the sink

Figure 2: The concentration profile $R(z)$ changes shape drastically with varying $r_0$.  

Arteries/veins

Vascular remodelling
Living webs never rest
Flows are dynamic

Internal mechanisms produce fluctuations on the flow. In the brain, neural activity entrains the vascular system.
Flows are dynamic

Internal mechanisms produce fluctuations on the flow. In the brain, neural activity entrains the vascular system.
Fluctuations in flow networks - whole brain
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Qinguang Zhang, P. Drew, Nature neuroscience
Hemodynamic signals and neural activity were strongly coupled for periods of high neural activity, but that correlation broke down during rest.

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*Patrick Drew’s Lab: A. Winder et al., Nat. Neuroscience, 20, 1761 (2017)*
Spontaneous fluctuations in cerebral blood volume and vessel diameter persisted even when neuronal activity was blocked, it suggests a non-neuronal origin for spontaneous CBV fluctuations!

Spontaneous fluctuations in cerebral blood volume and vessel diameter persisted even when neuronal activity was blocked, it suggests a non-neuronal origin for spontaneous CBV fluctuations!

Weak correlations between hemodynamic signals and ongoing neural activity during the resting state

Aaron T. Winder¹,², Christina Echagarruga³, Qingguang Zhang¹,² and Patrick J. Drew¹,²,³,⁴

Spontaneous fluctuations in hemodynamic signals in the absence of a task or overt stimulation are used to infer neural activity. We tested this coupling by simultaneously measuring neural activity and changes in cerebral blood volume (CBV) in the somatosensory cortex of awake, head-fixed mice during periods of true rest and during whisker stimulation and volitional whisking. We found that neurovascular coupling was similar across states and that large, spontaneous CBV changes in the absence of sensory input were driven by volitional whisker and body movements. Hemodynamic signals during periods of rest were weakly correlated with neural activity. Spontaneous fluctuations in CBV and vessel diameter persisted when local neural spiking and glutamatergic input were blocked, as well as during blockade of noradrenergic receptors, suggesting a non-neuronal origin for spontaneous CBV fluctuations. Spontaneous hemodynamic signals reflect a combination of behavior, local neural activity, and putatively non-neural processes.
Weak correlations between hemodynamic signals and ongoing neural activity during the resting state

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A minimal model for excitable flow networks

A network of linear resistors has one unique solution for each boundary condition, we need a different model that allow for volume accumulations and that can support traveling waves:
A minimal model for excitable flow networks

A network of linear resistors has one unique solution for each boundary condition, we need a different model that allow for volume accumulations and that can support traveling waves:

Volume at node $i$: $V_i$
Pressure at node $i$: $P_i$
A minimal model for excitable flow networks

A network of linear resistors has one unique solution for each boundary condition, we need a different model that allows for volume accumulations and that can support traveling waves:

Volume at node $i$: $V_i$
Pressure at node $i$: $P_i$

Current between nodes $i$ and $j$:

$$I_{ij} = \begin{cases} 
V_i^2 \Gamma(P_i - P_j) & \text{if } P_i > P_j \\
V_j^2 \Gamma(P_i - P_j) & \text{if } P_i < P_j 
\end{cases}$$
A minimal model for excitable flow networks

A network of linear resistors has one unique solution for each boundary condition, we need a different model that allow for volume accumulations and that can support traveling waves:

Volume at node $i$: $V_i$
Pressure at node $i$: $P_i$

Current between nodes $i$ and $j$:

$$I_{ij} = \begin{cases} V_i^2 \Gamma(P_i - P_j) & \text{if } P_i > P_j \\ V_j^2 \Gamma(P_i - P_j) & \text{if } P_i < P_j \end{cases}$$

Dispersive relation:

$$V_i - \tilde{V} = \alpha \hat{L}_{ij} P_j$$

Graph Laplacian ($\sim -\nabla^2$): $\hat{L}_{ij}$
Self-sustained oscillations

Constant pressure boundary conditions

Pulses travel from one source to another and recycle

Non-linearities + dispersive relation leads to complex dynamics

Self-sustained oscillations
Self-sustained oscillations

Constant pressure boundary conditions

Pulses travel from one source to another and recycle

Non-linearities + dispersive relation leads to complex dynamics
Phase diagram: regions with or without oscillations

\[
\sqrt{\sum (V_n - \langle V_n \rangle)^2}
\]
Phase diagram: regions with or without oscillations

\[\sqrt{\sum_{n} (V_n - \langle V_n \rangle)^2}\]
Different number of sources, topologies, distribution of linear edges... give different oscillations:
Quantifying the effect of different topologies and conductivities

Frequency increases with the number of shortcuts until all oscillations disappear. Analogous behavior when more edges become linear.
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Quantifying the effect of different topologies and conductivities

Frequency increases with the number of shortcuts until all oscillations disappear. Analogous behavior when more edges become linear.

What is the measure of the network that predicts this behavior?
Introducing an effective distance to account for the frequency increase

Adding shortcuts between randomly chosen nodes or changing the conductivities of some edges make the network “shorter” increasing the frequency of the oscillations. This effective distance is proportional to the escape probability of a random walk in the network.
We can now try the model using the real surface arteriole network of a mouse, outputs are the penetrating arterioles. We impose constant pressure at the inputs and outputs. The same phenomenological nonlinear conductivities produce spontaneous fluctuations.
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Summary

Optimal living webs
Flow networks have to do their job well, and they have been designed to do so

Building the living webs
Growth allows the system to find the global minimum for dissipation based only on local information: a new optimization method

Living webs never rest
It is possible to build AC currents out of DC resistors whose frequency depends on the network topology
Towards universal principles

Plants, slime molds, our own venation

Hierarchical, full of nested loops: common principles, but also differences in the architecture. Inspiration about other living (or dead) systems
THE PHYSIOLOGICAL PRINCIPLE OF MINIMUM WORK. I.
THE VASCULAR SYSTEM AND THE COST OF BLOOD VOLUME

BY CECIL D. MURRAY

DEPARTMENT OF BIOLOGY, Bryn Mawr College
Communicated January 26, 1928

Introduction.—Physiological organization, like gravitation, is a "stubborn fact," and it is one task of theoretical physiology to find quantitative laws which describe organization in its various aspects. Just as the laws of thermodynamics were known before the kinetic theory of gases was developed, so it is not impossible that some quantitative generalizations may be arrived at in physiology which are independent of the discrete mechanisms in living things, but which apply to organic systems considered statistically. One such generalization is the principle of the maintenance of steady states—a principle which furnishes definite equations (of the type indicating equality of intake and output of elementary substances) applicable to the hypothetical normal individual. The purpose of these studies is to discuss the possible application of a second principle, the principle of minimum work, to problems concerning the operation of physiological systems.

$r_p^3 = \sum r^3_d$
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