

Detangling the vascular web: Loops, hierarchies, and the quest for Nature's design principles

Eleni Katifori

Department of Physics and Astronomy, University of Pennsylvania

Acknowledgements

Students and post-docs

Jana Lasser
Henrik Ronellenfitsch
Desislava Todorova
Jonathan Dawson
Johannes Gräwer

Other collaborators

Carl Modes
Marcelo Magnasco
Kaare Jensen
Douglas Daly

Funding

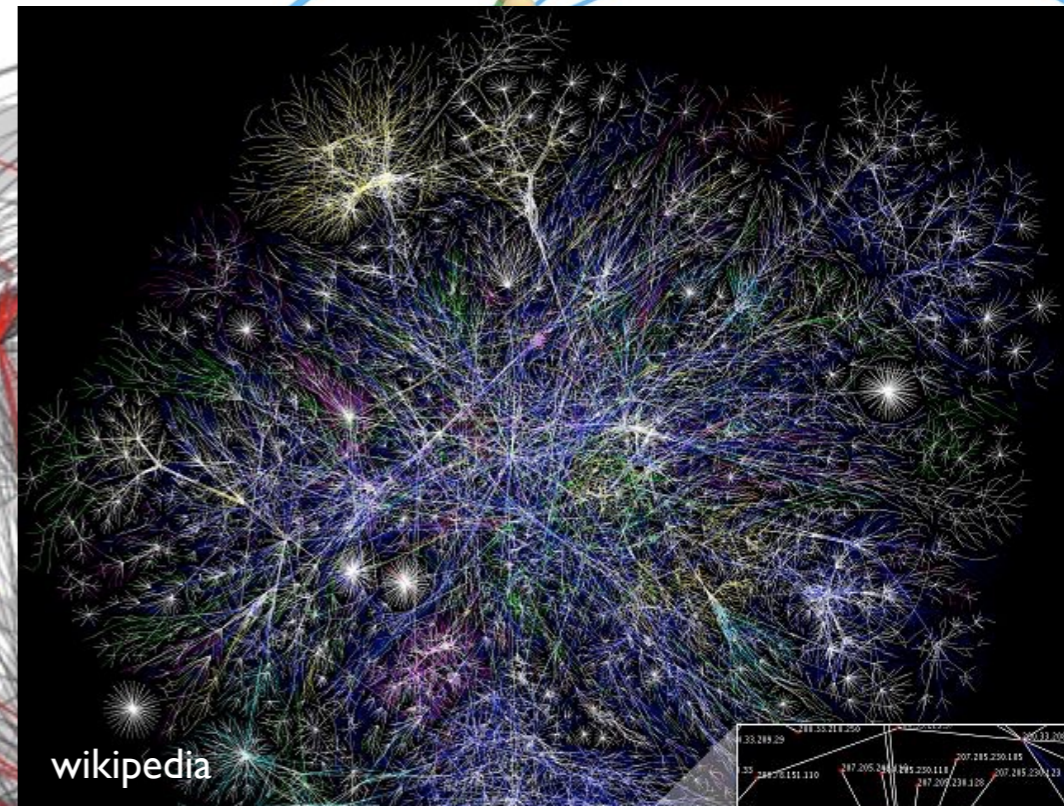
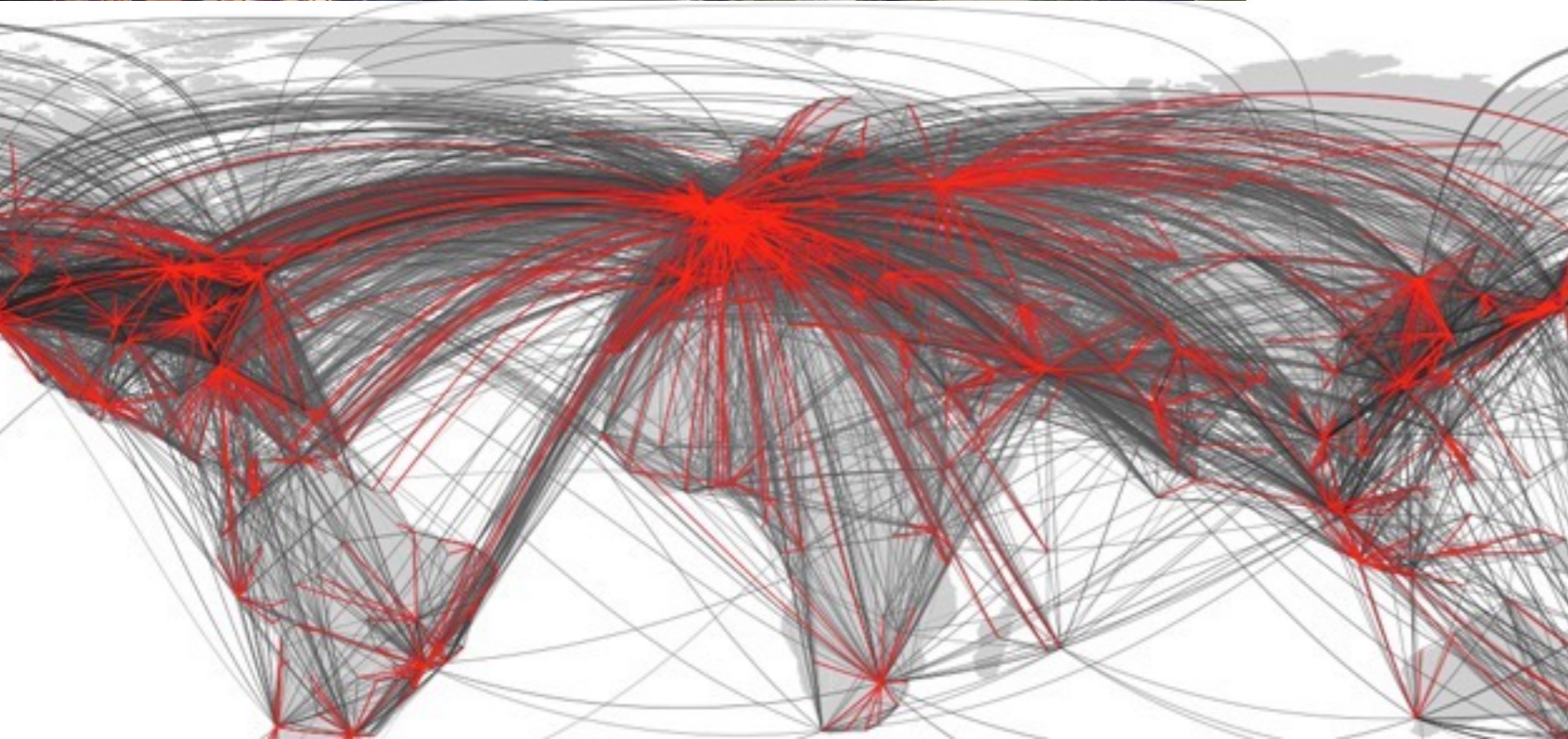
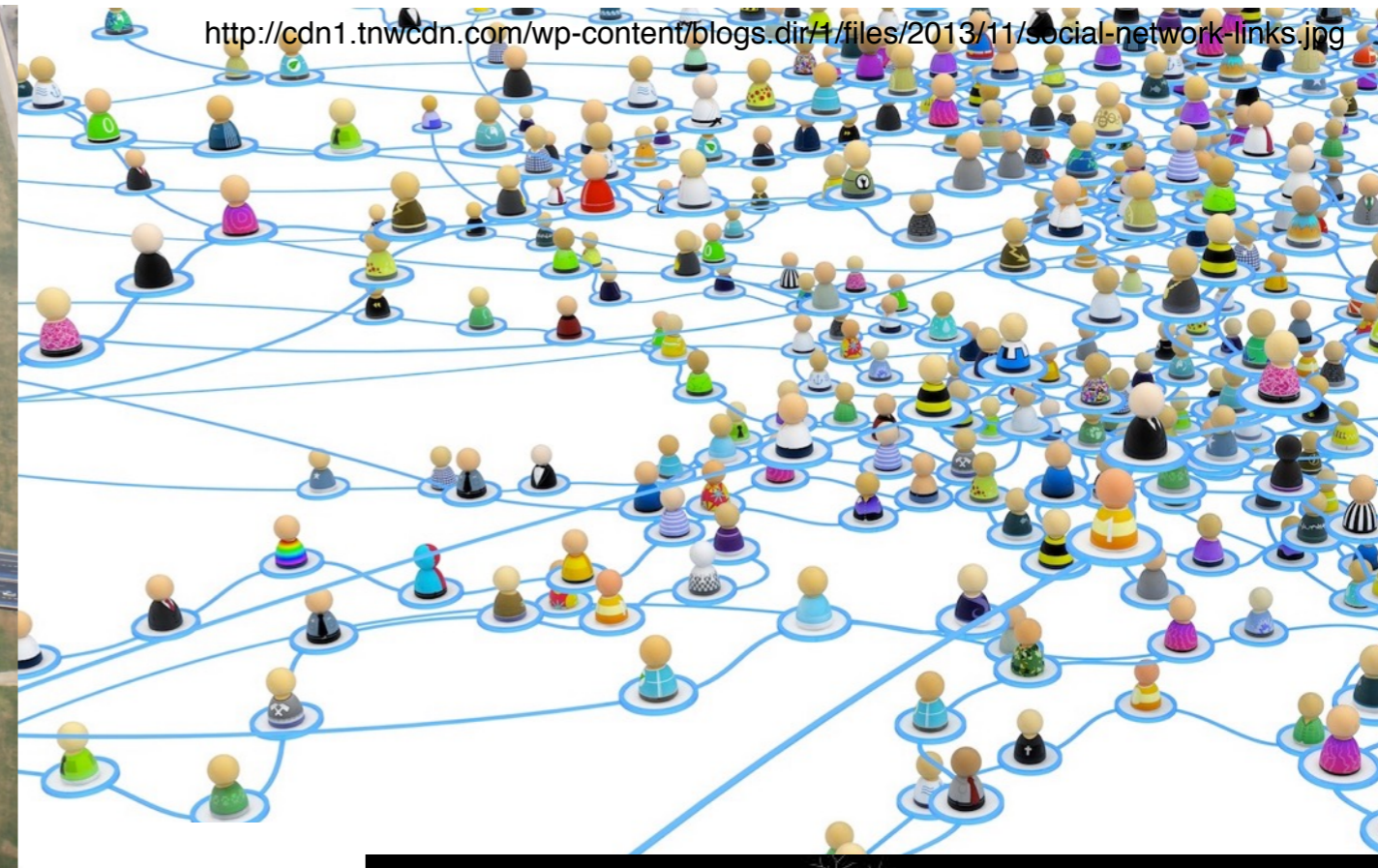


MAX-PLANCK-GESELLSCHAFT

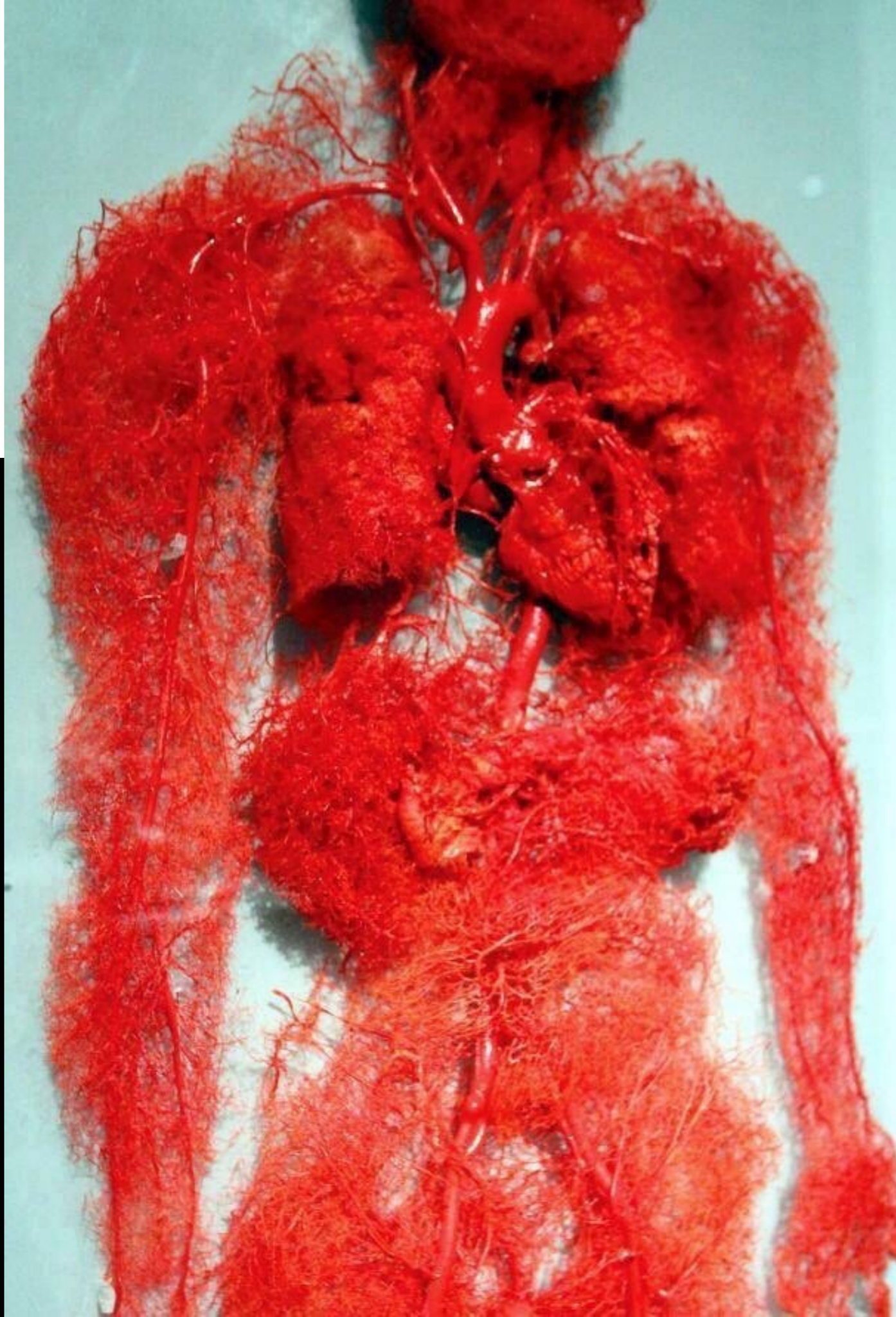
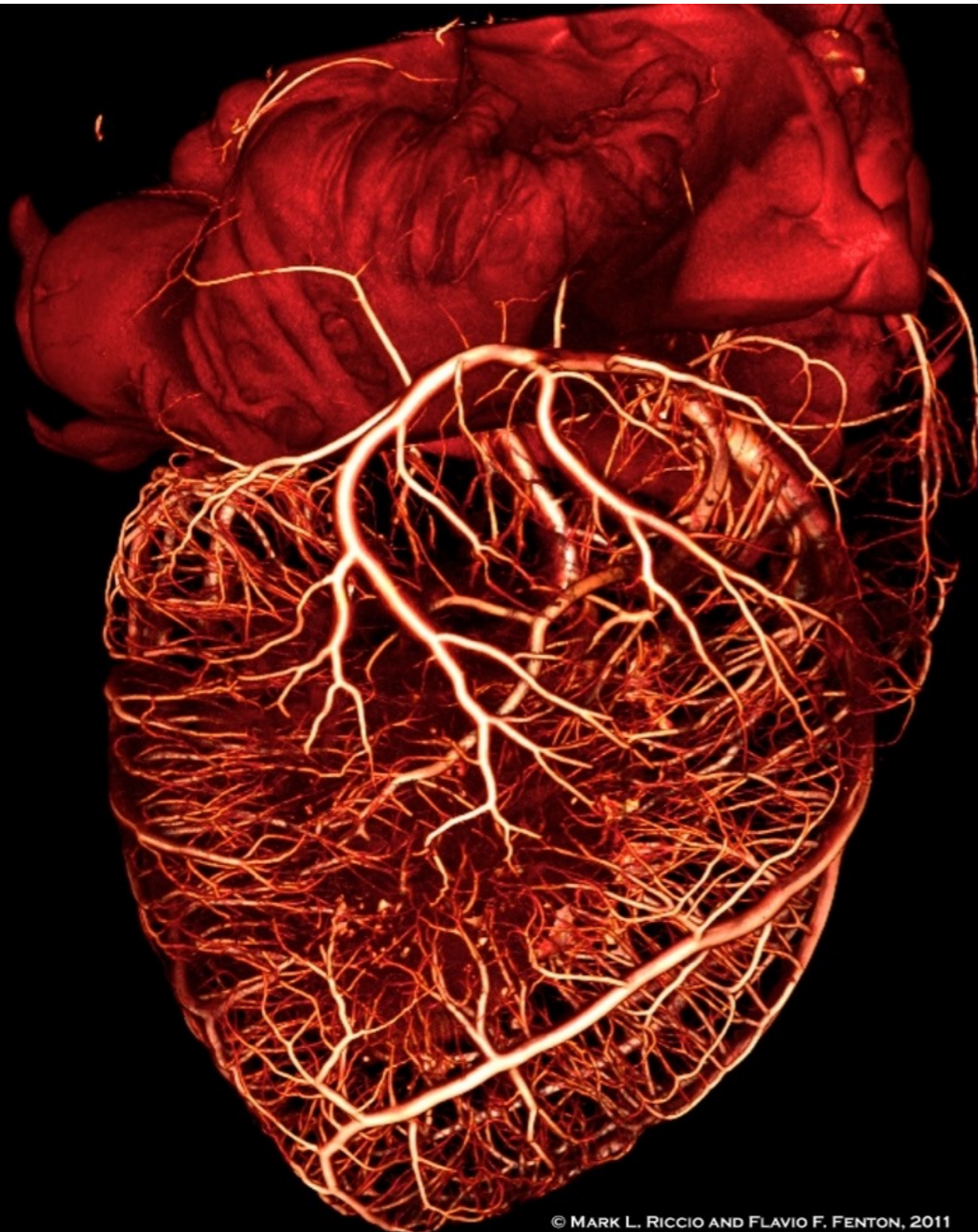
BURROUGHS
WELLCOME
FUND 



We live in a highly interconnected world



**And yet, we don't
have to go further
than our own bodies**



Diffusion is not enough

How far can diffusion get you?

Not very far!

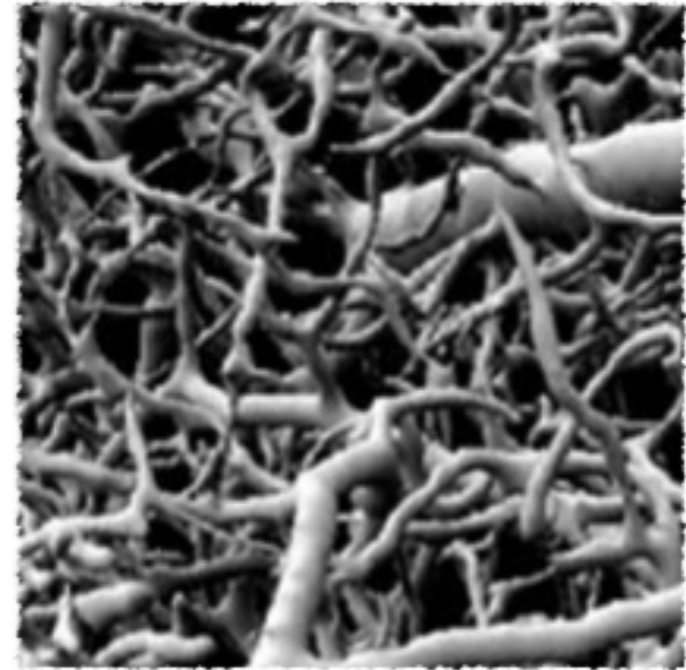
Diffusion of O₂ in water

10 μm (cell): 30 ns

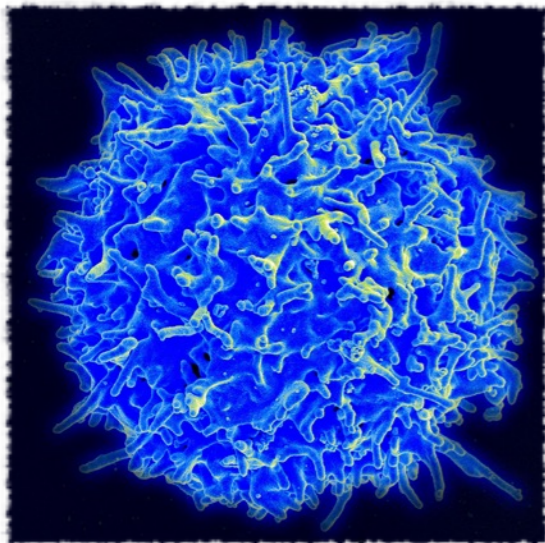
100 μm : 3 s

1 mm : 5 min

Distance between
capillaries: < 40 μm

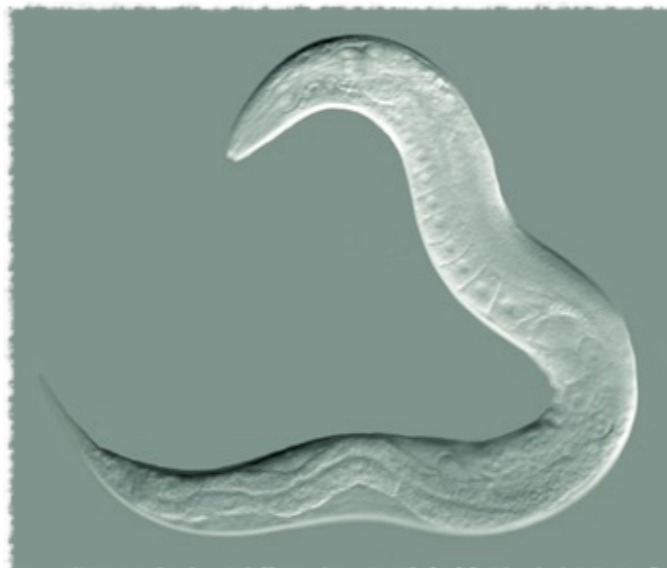


T-cell 10 μm



By NIAID/NIH - NIAID Flickr's photostream, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=18233598>

nematode 1 mm



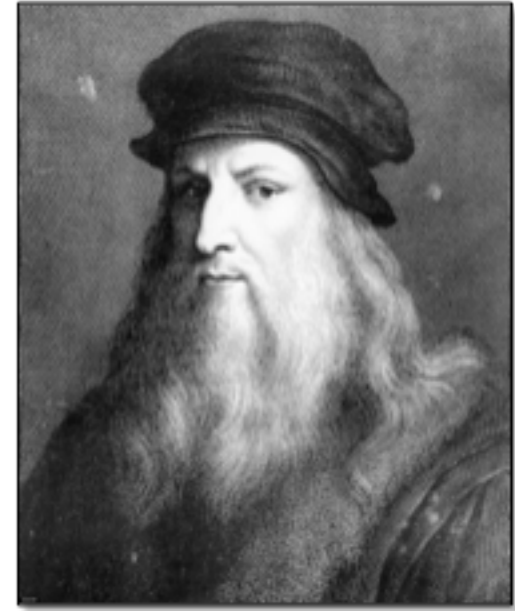
By Bob Goldstein, UNC Chapel Hill

mouse 10cm



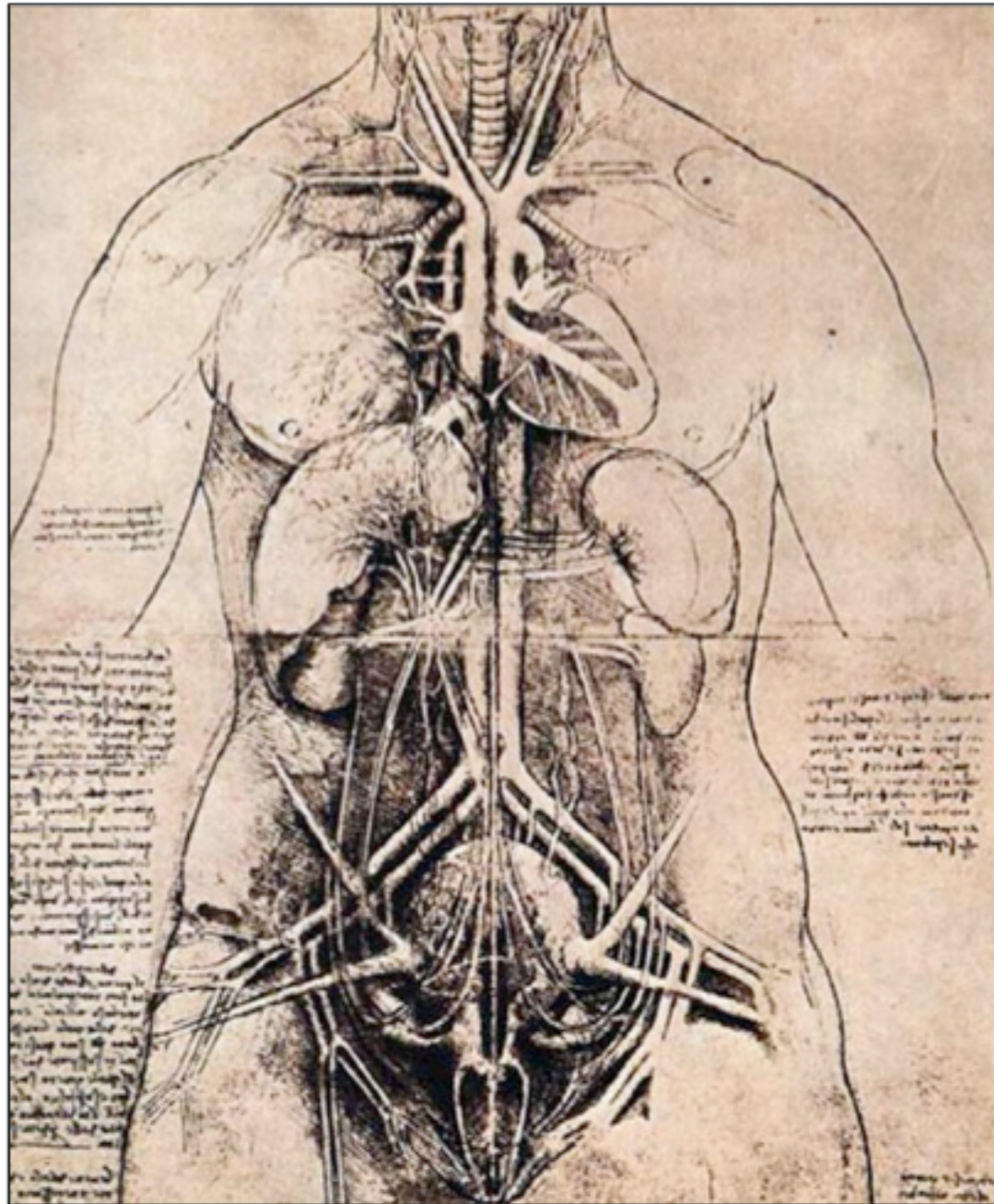
<http://www.domyownpestcontrol.com/images/content/mouse.jpg>

Da Vinci and natural transport systems

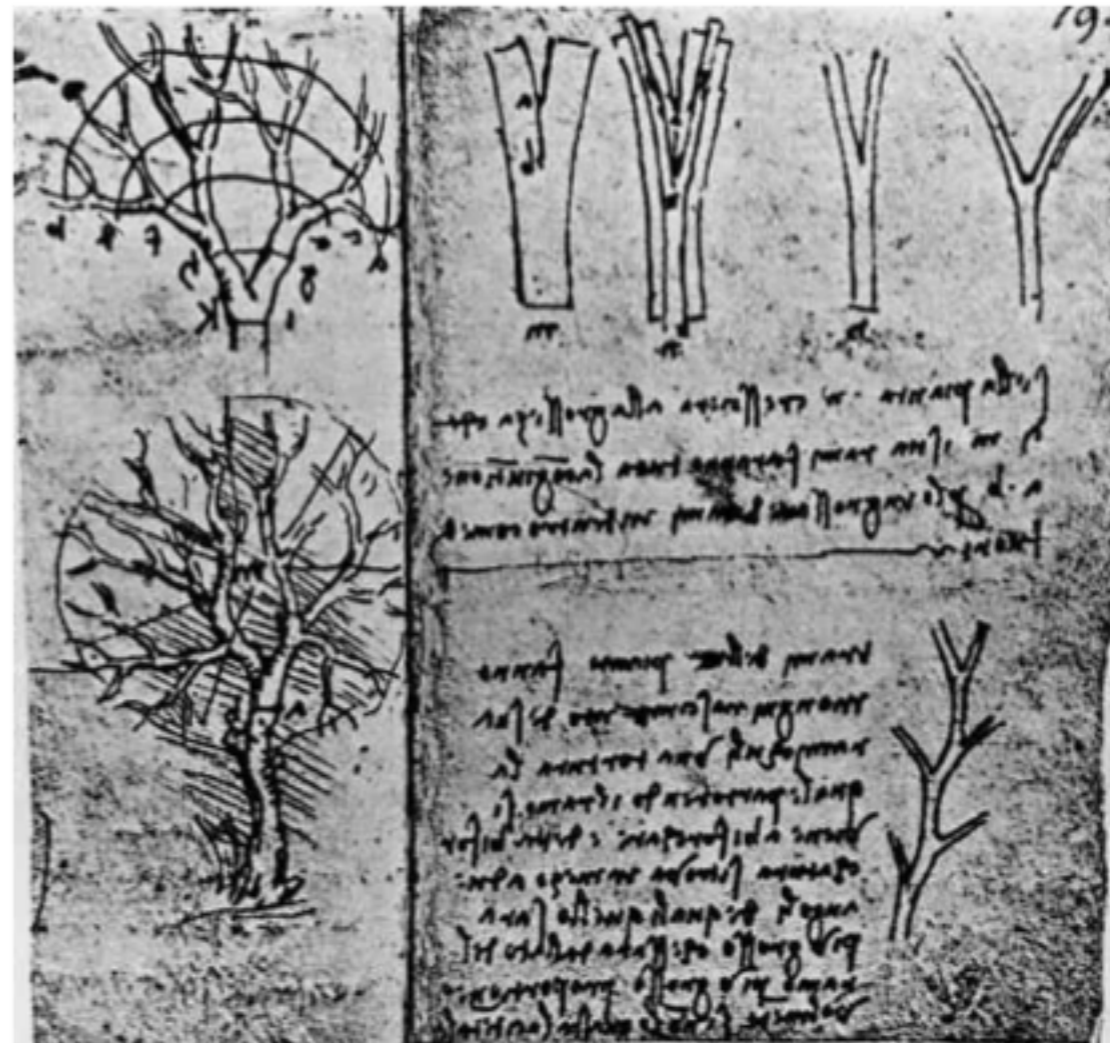


Leonardo da Vinci
1452-1519

"[The earth]'s blood [is] the veins of the waters."



"All the branches of a tree at every stage of its height when put together are equal in thickness to the trunk."



Why do vascular systems look the way they do?

Murray's law:

Animal vasculature minimizes energetic costs of dissipation

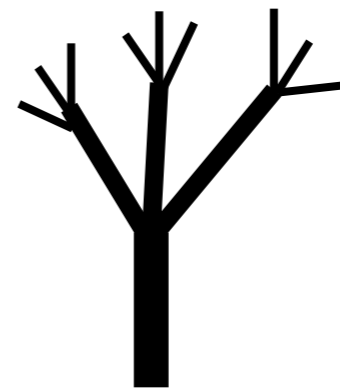
*THE PHYSIOLOGICAL PRINCIPLE OF MINIMUM WORK. I.
THE VASCULAR SYSTEM AND THE COST OF BLOOD VOLUME*

BY CECIL D. MURRAY

DEPARTMENT OF BIOLOGY, BRYN MAWR COLLEGE

Communicated January 26, 1926

$$r^3 = r_1^3 + r_2^3 + \dots + r_n^3$$

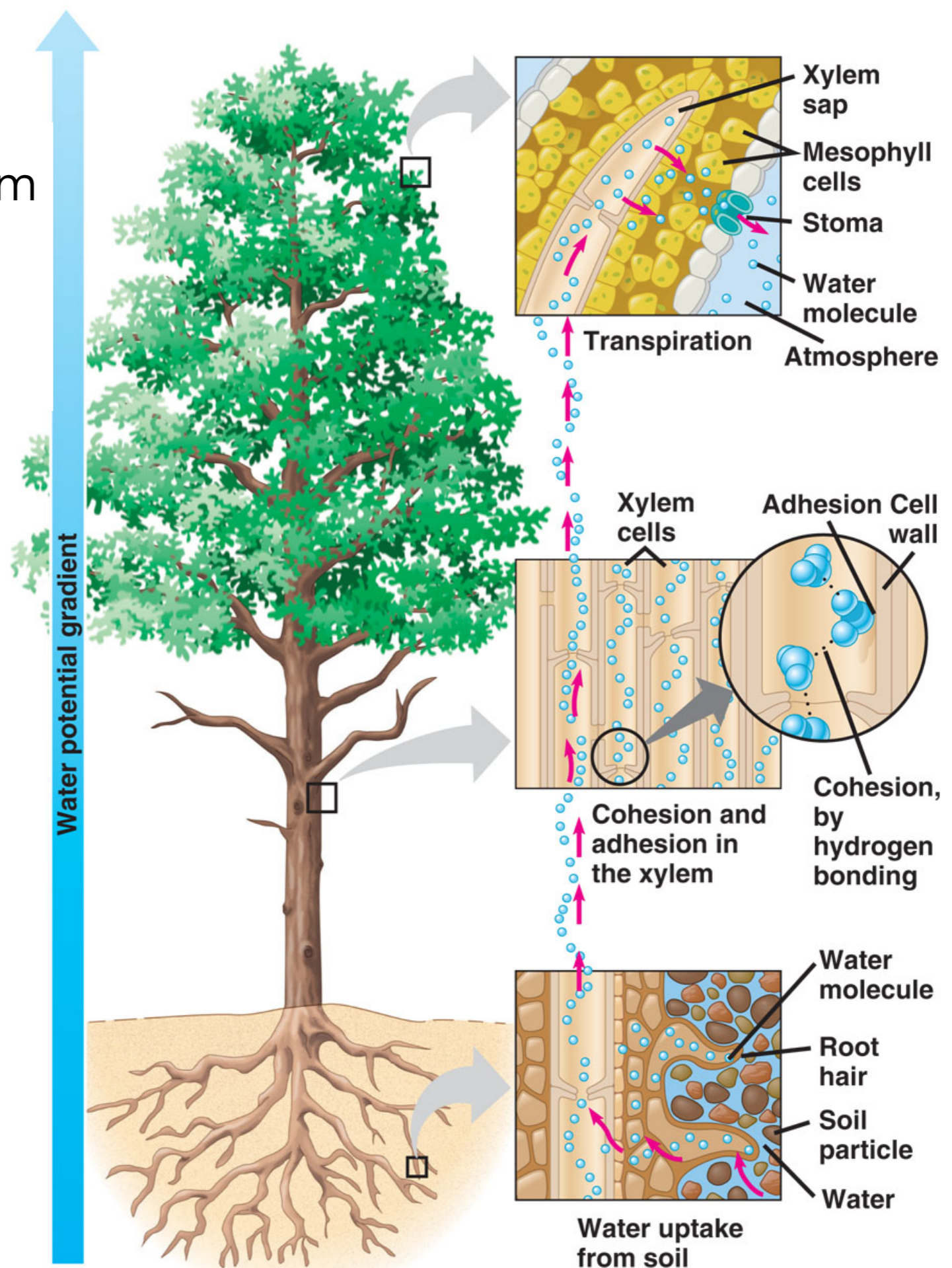


Optimality principles have been found to hold in several biological transport networks, both in plants and animals.

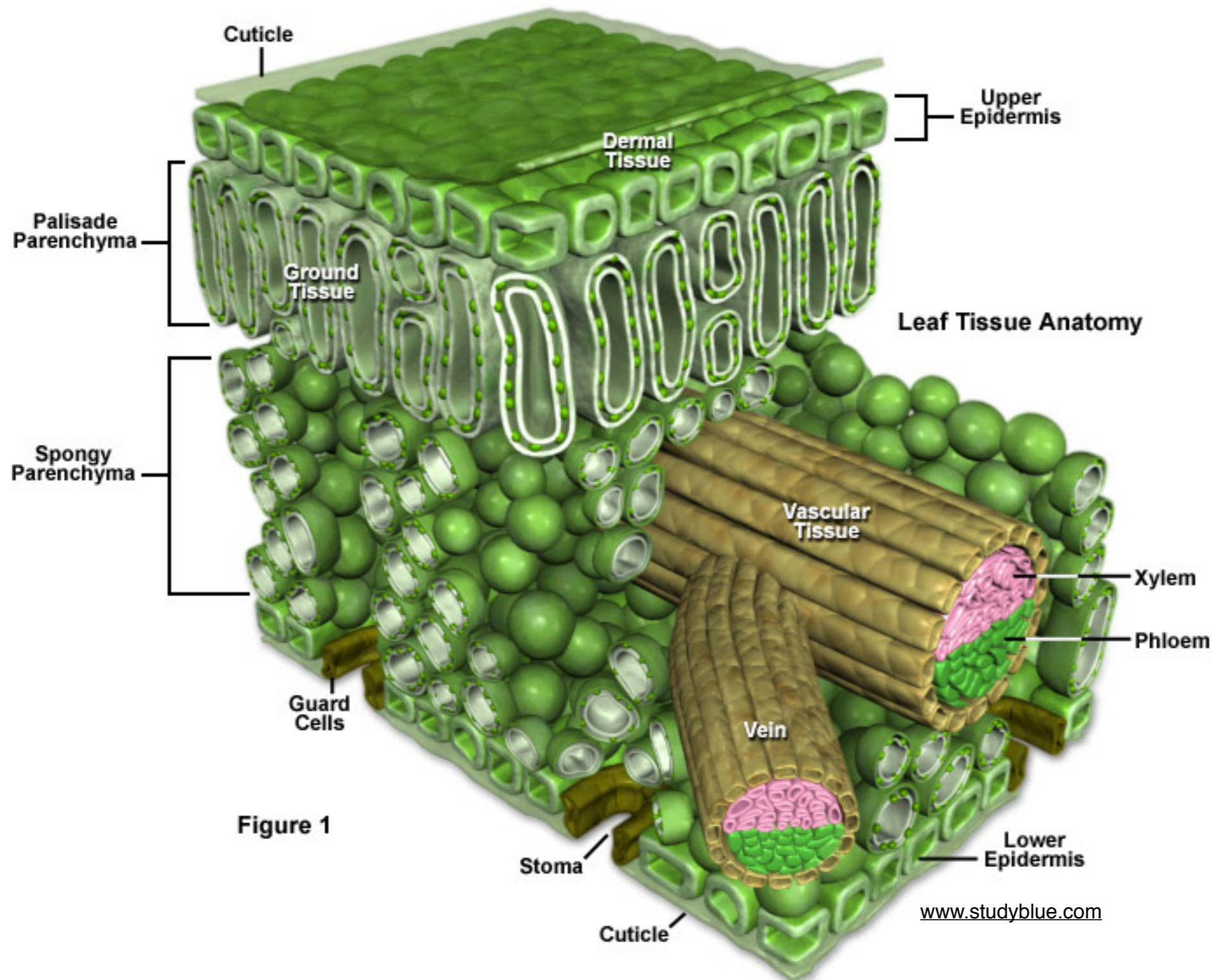
Plant vascular network: The xylem

-10 atm

Water column
under tension.
Dangers of cavitation
and embolisms



The leaf

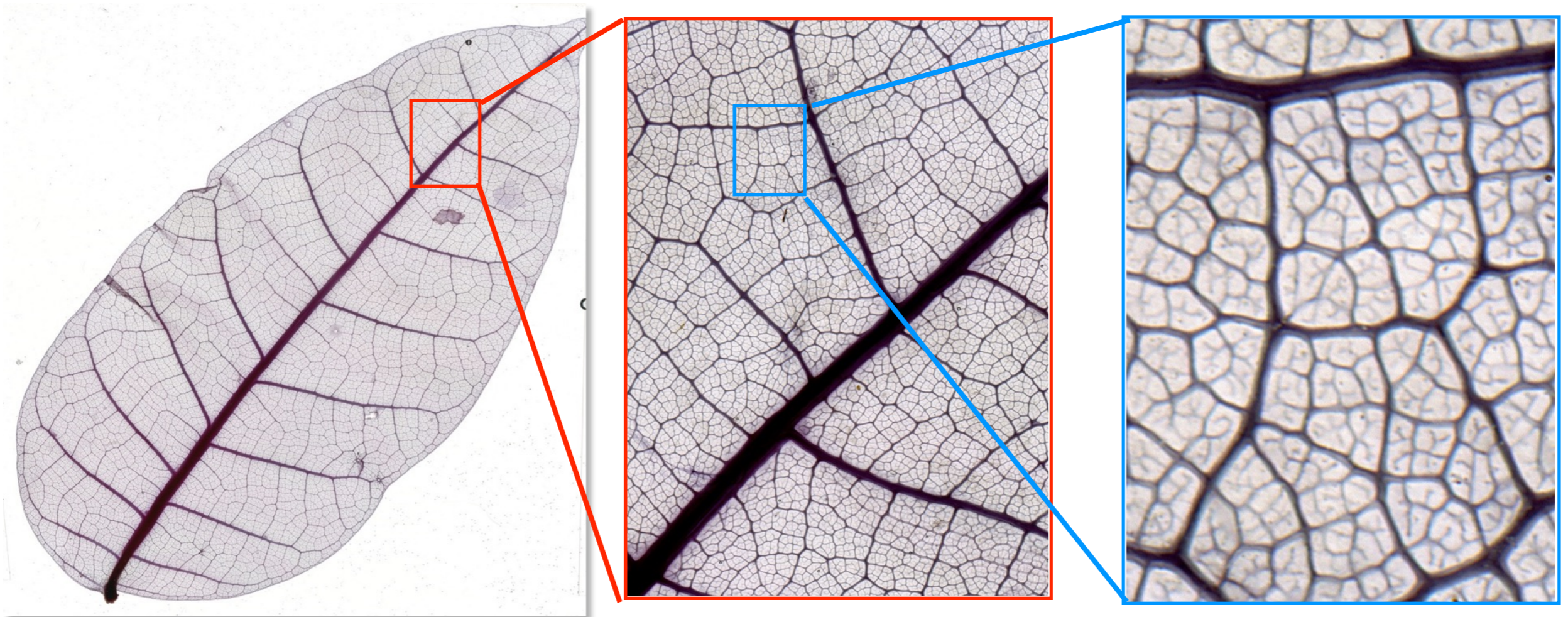


Photosynthetic efficiency is limited by water potential at the leaf.

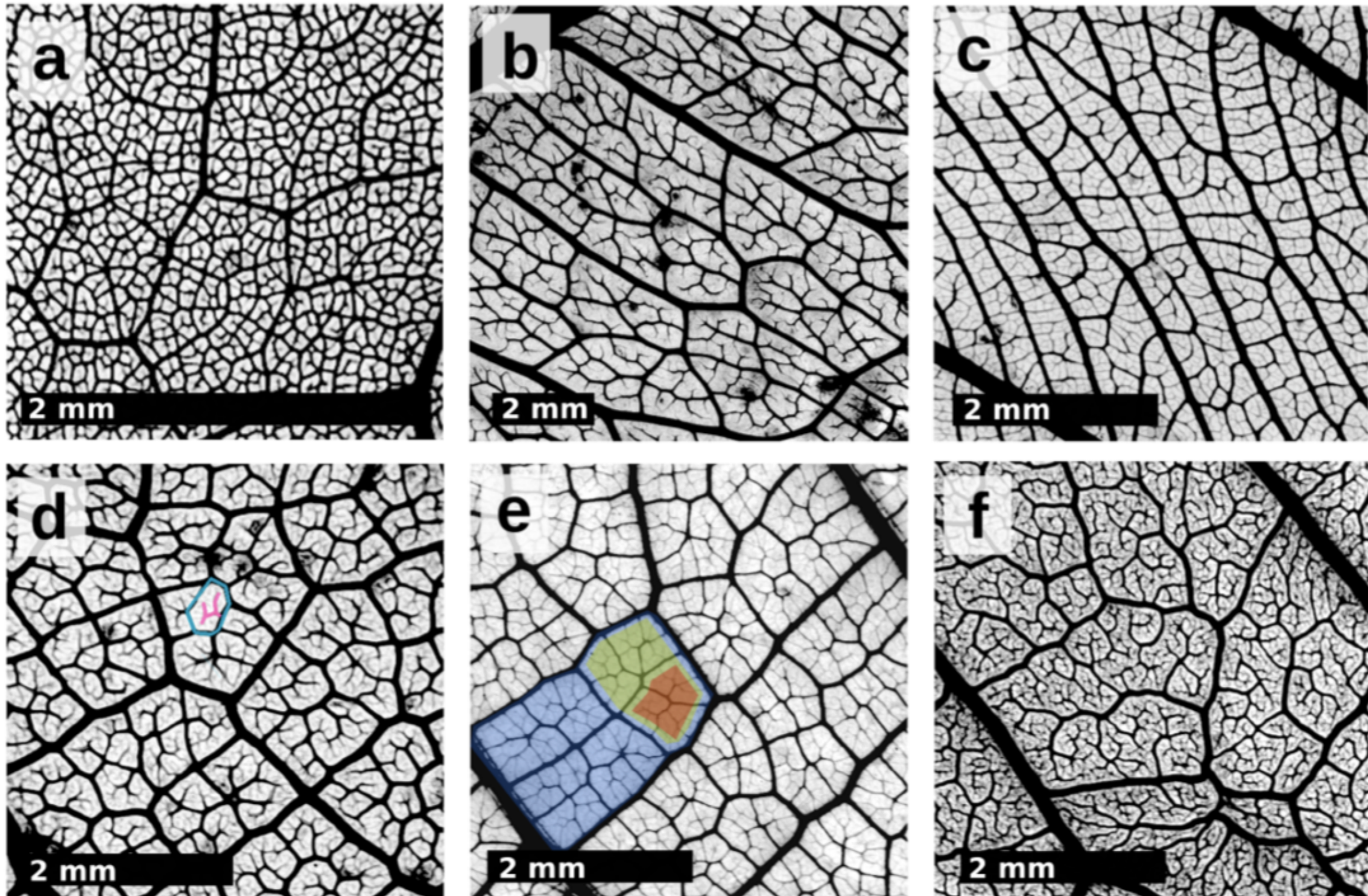
Leaf vascular architecture: Lots of Loops

Leaves are not trees...

Loops within loops within loops!

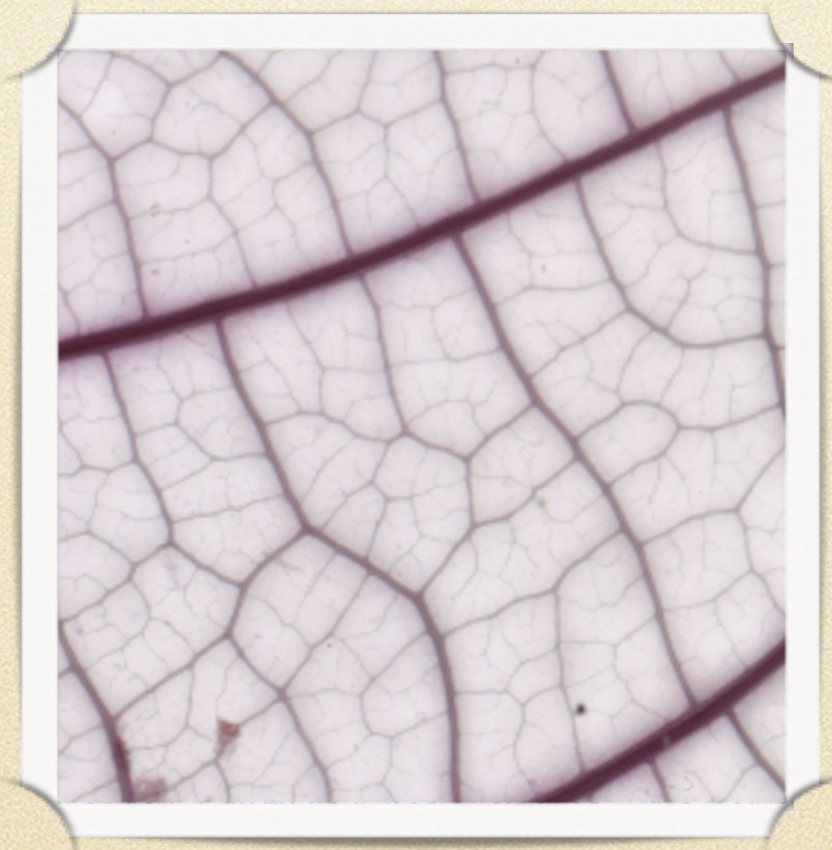


Many distinct venation types: hierarchically nested!

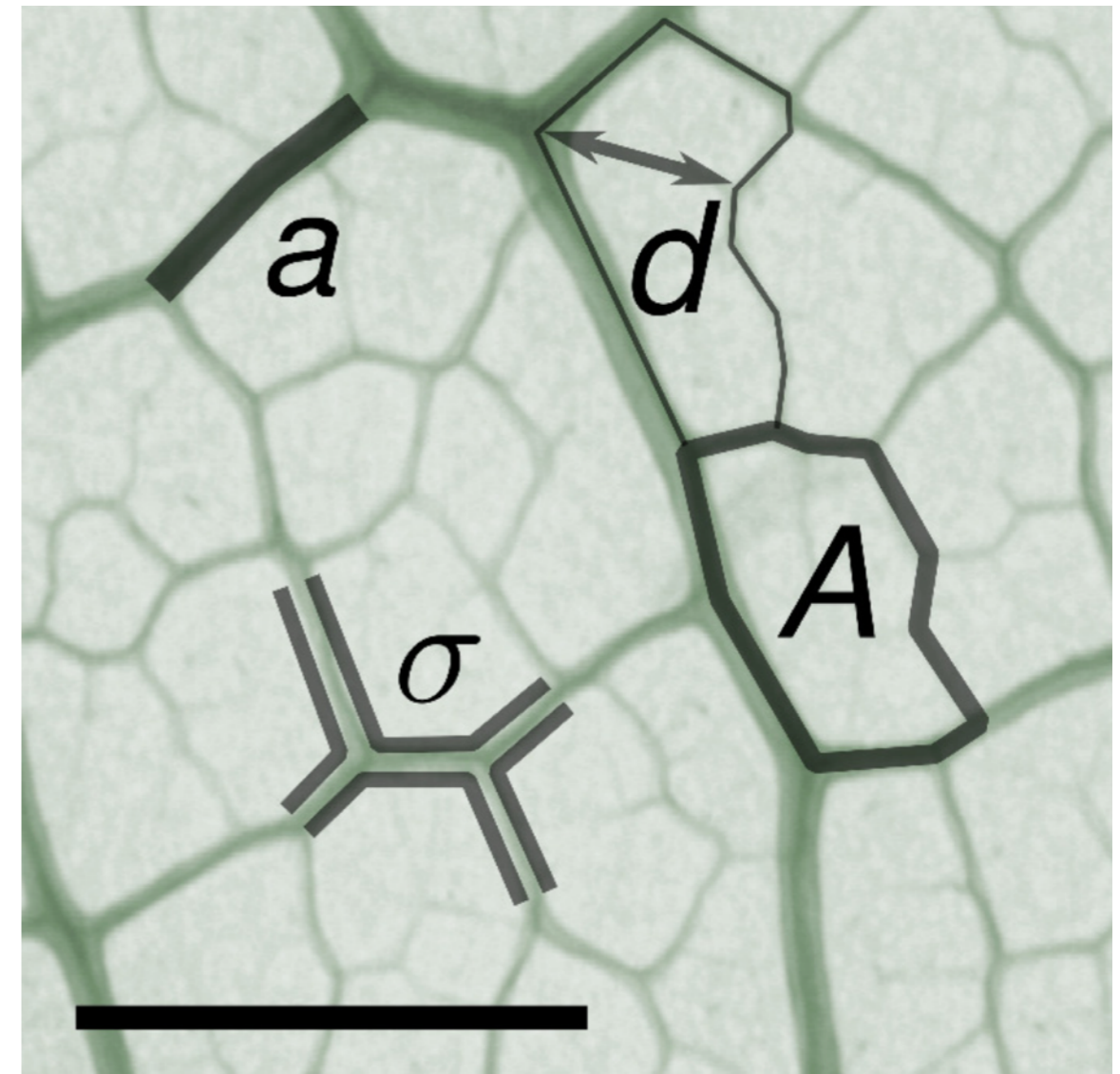
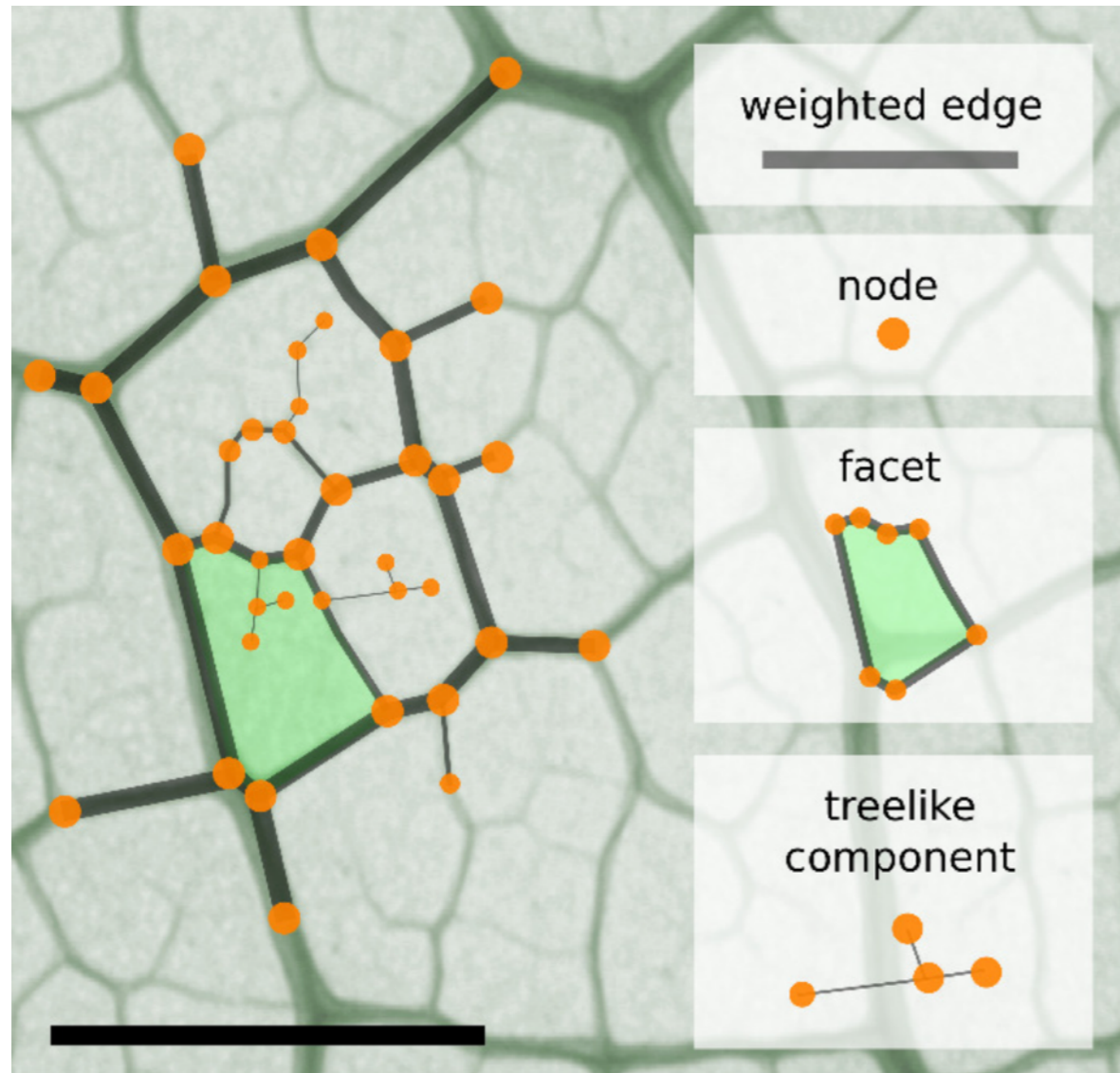


a *Protium ovatum*. b *Protium madagascariense*. c *Pouteria filipes*. d *Canarium betamponae*. A single areole is marked in blue, non-anastomosing highest order veins in red. e *Brosimum guianensis*. The hierarchical nesting of loops is highlighted. f *Protium subserratum*.

Measuring hierarchical nestedness

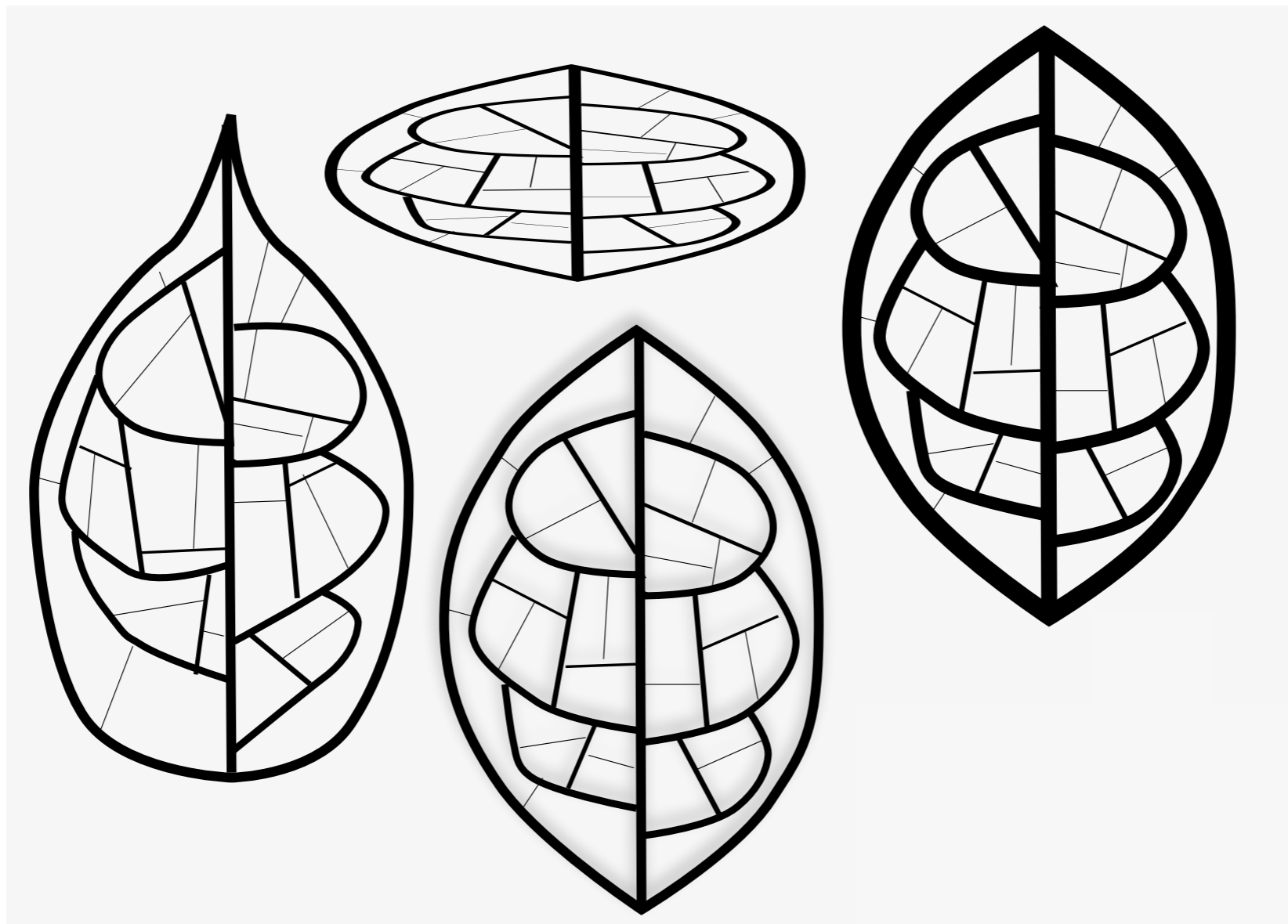


Studying the geometry of the networks



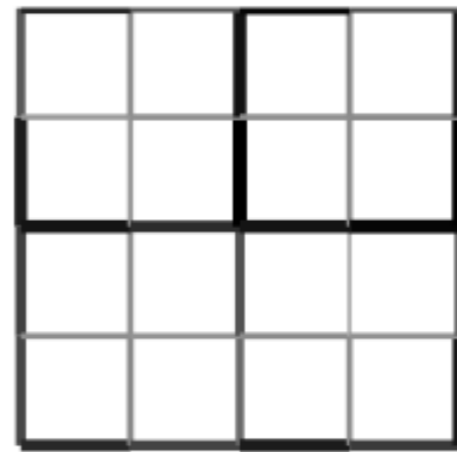
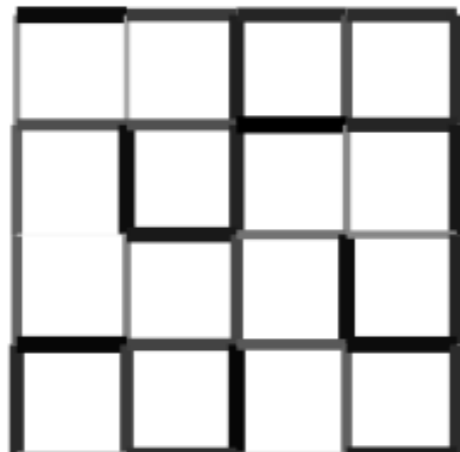
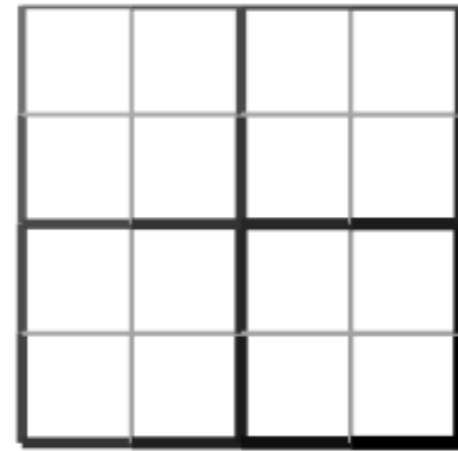
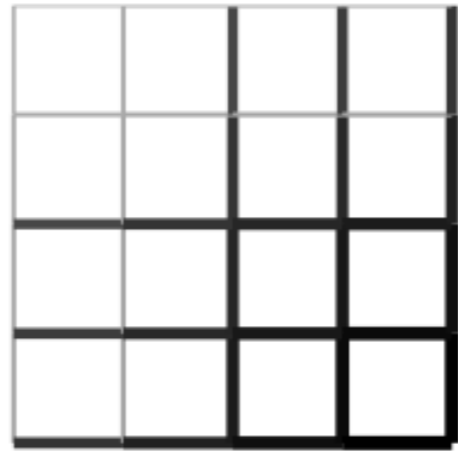
Studying the topology of the networks

Information about geometry and weight is decoupled
only topology and sort order of edges matters

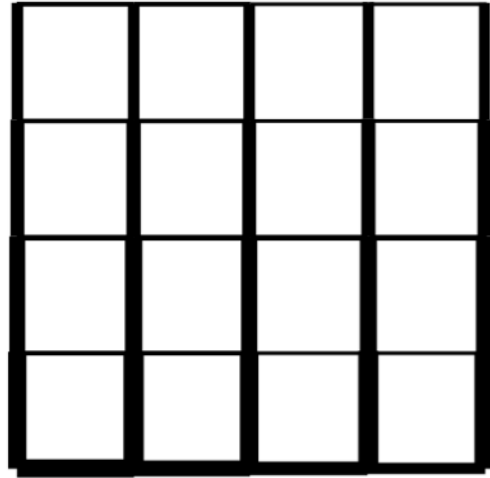


Studying the topology of the networks

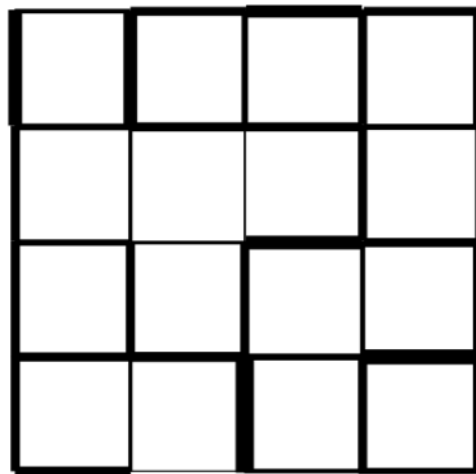
Vein density, vein width distribution, vein density, junction geometry ...
What about connectivity of weighted edges?



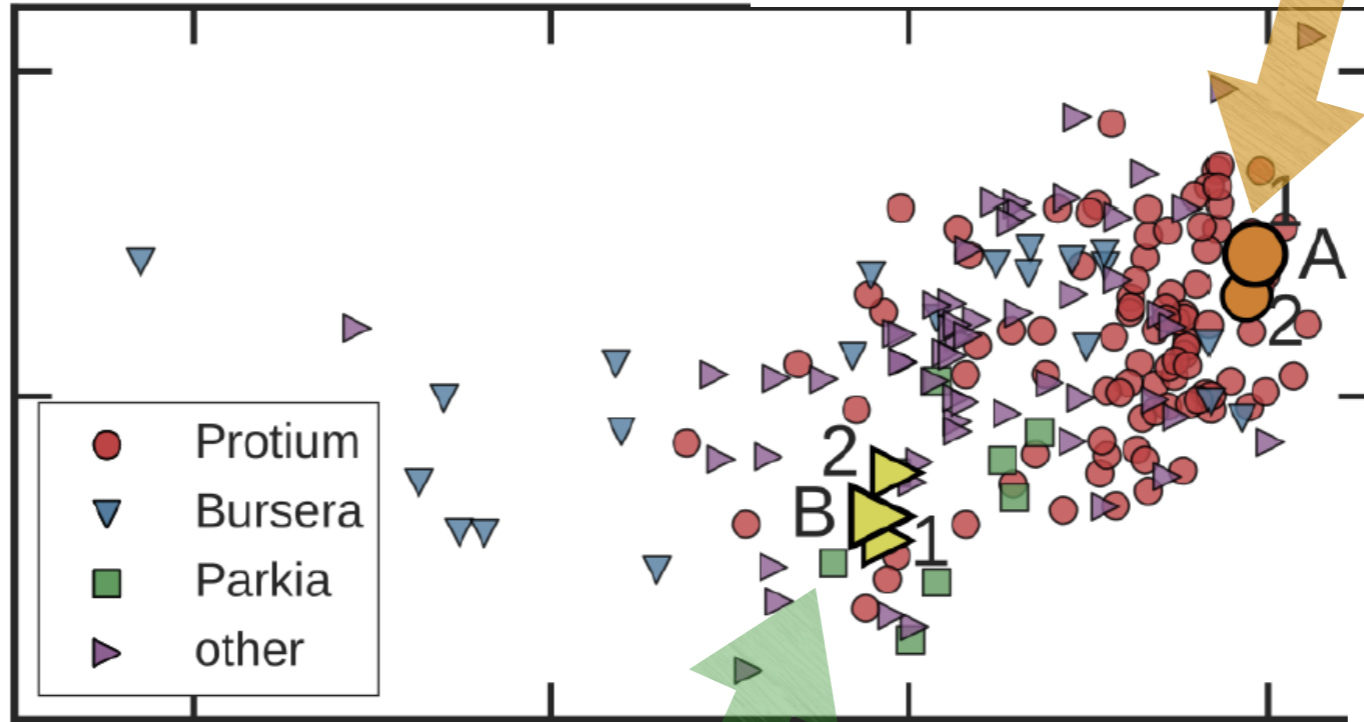
Leaf fingerprinting



topological length
4.0
3.5



(a)

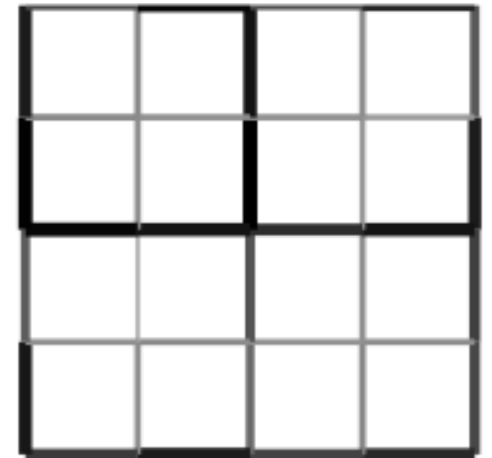
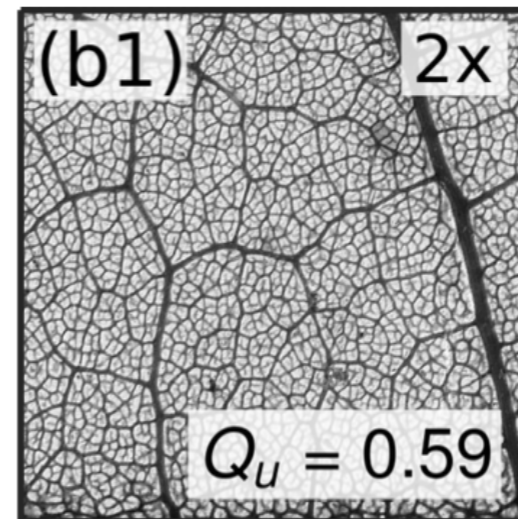
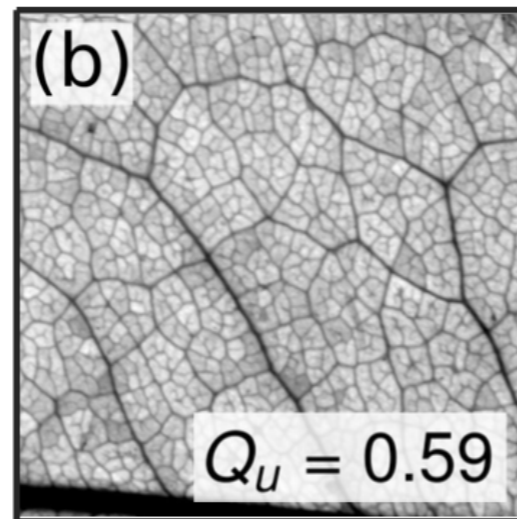
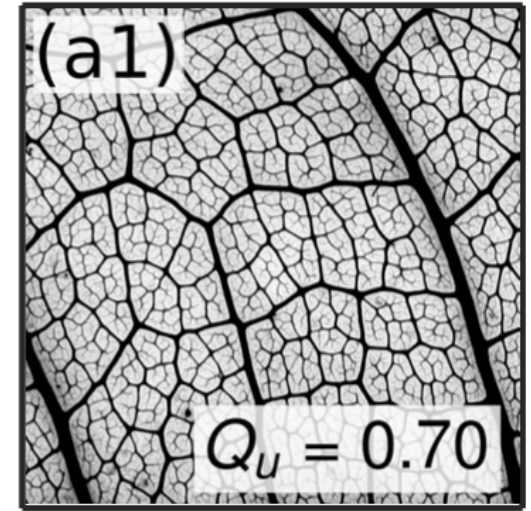
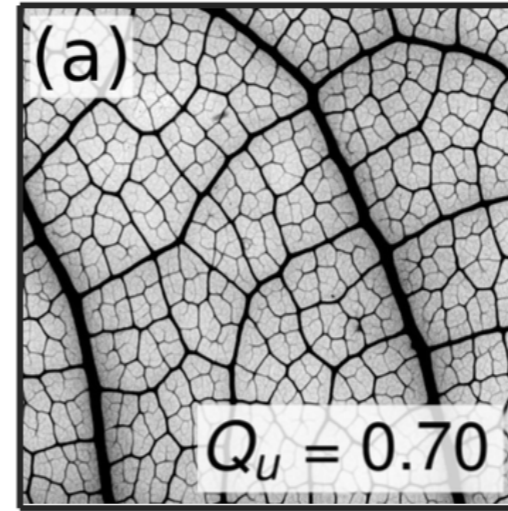


Dalbergia miscolobium

Protium heptaphyllum 0.7

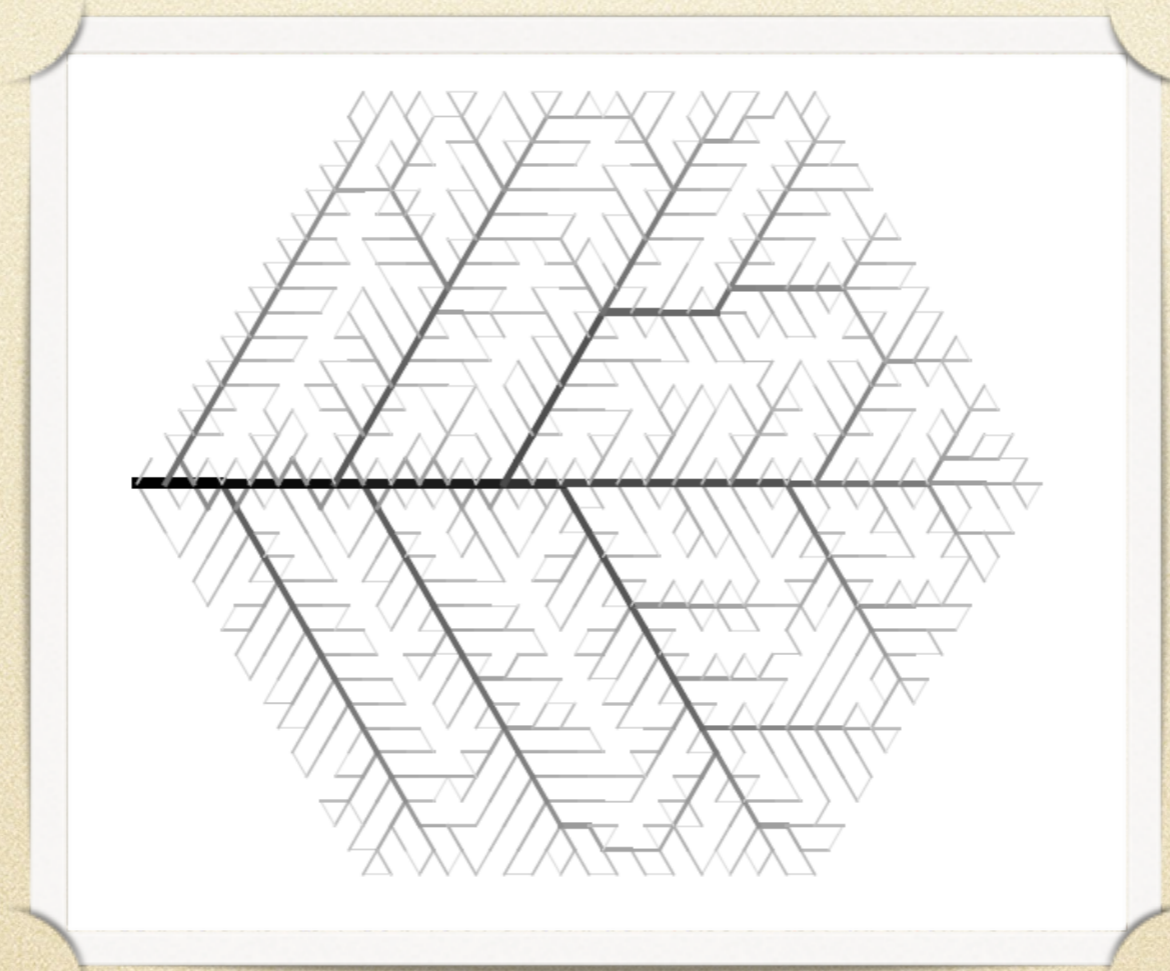
Protium grandifolium

Protium cuneatum

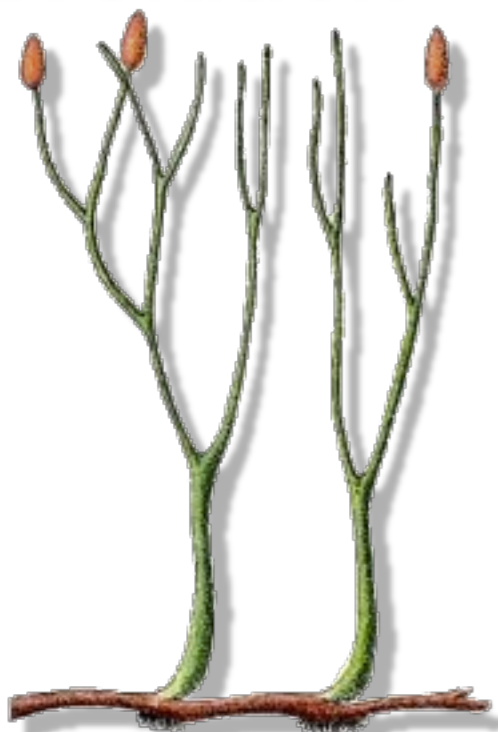


Hierarchically nested loops are a distinctive feature of leaf vasculature.

Why loops? Exploring optimality principles



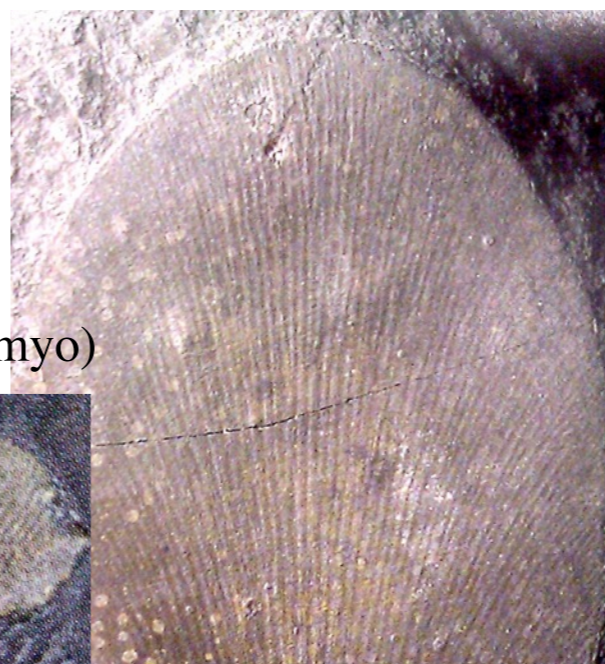
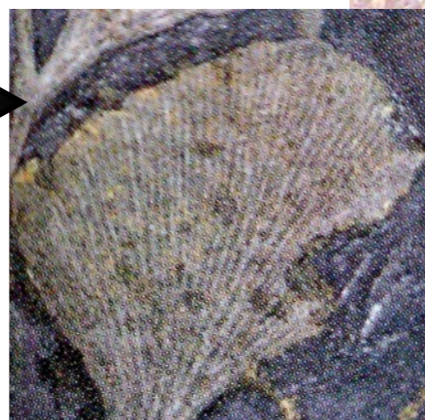
Evolution



First plants:
dichotomously branching

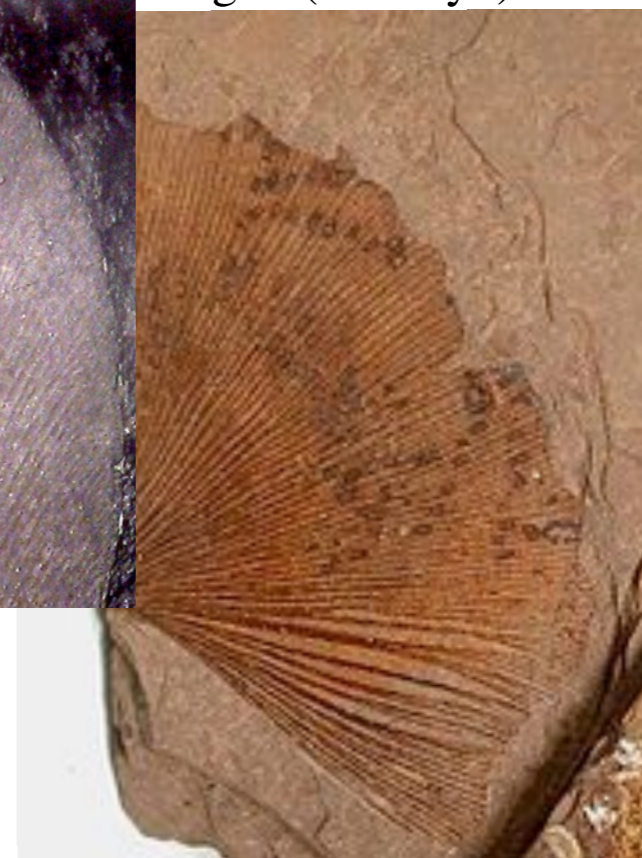


First leaves:
no loops!
Adiantites (330 myo)



Gangamopteris
(300 myo)

Ginkgo (200 myo)

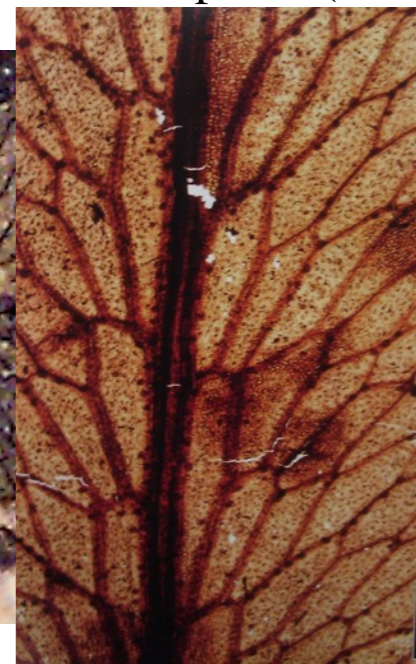


First simple anastomosing patterns



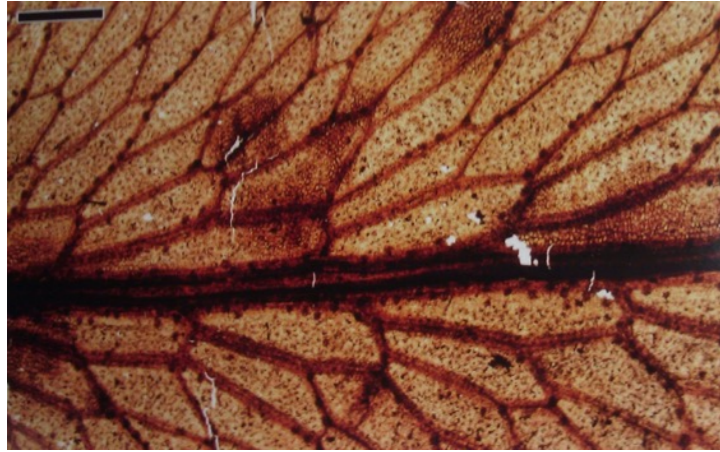
Glossopteris

Barthelopteris (250 myo)



Evolution

Barthelopteris (250 myo)



Evolution of
hierarchical structures

...

Modern angiosperms

(140 myo)

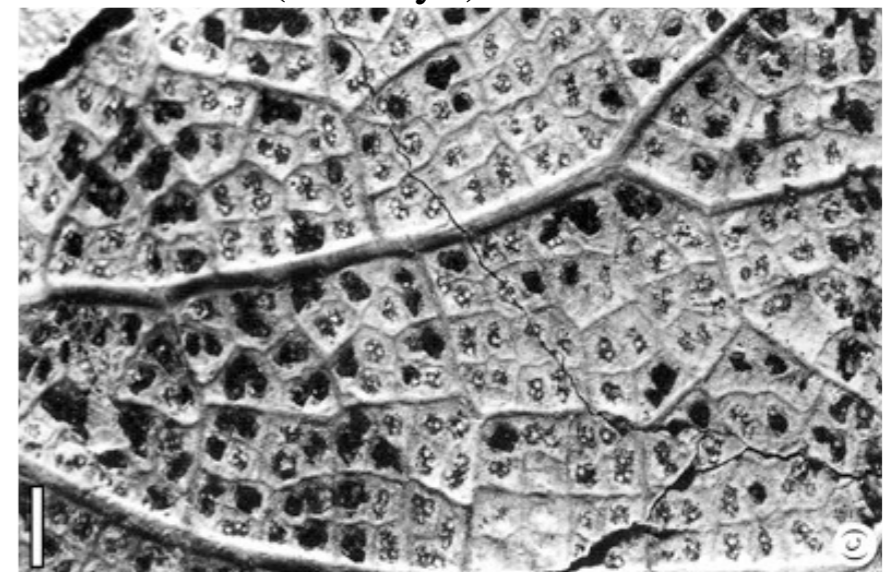


Convergent evolution:

Ferns independently evolved reticulate vascular structures

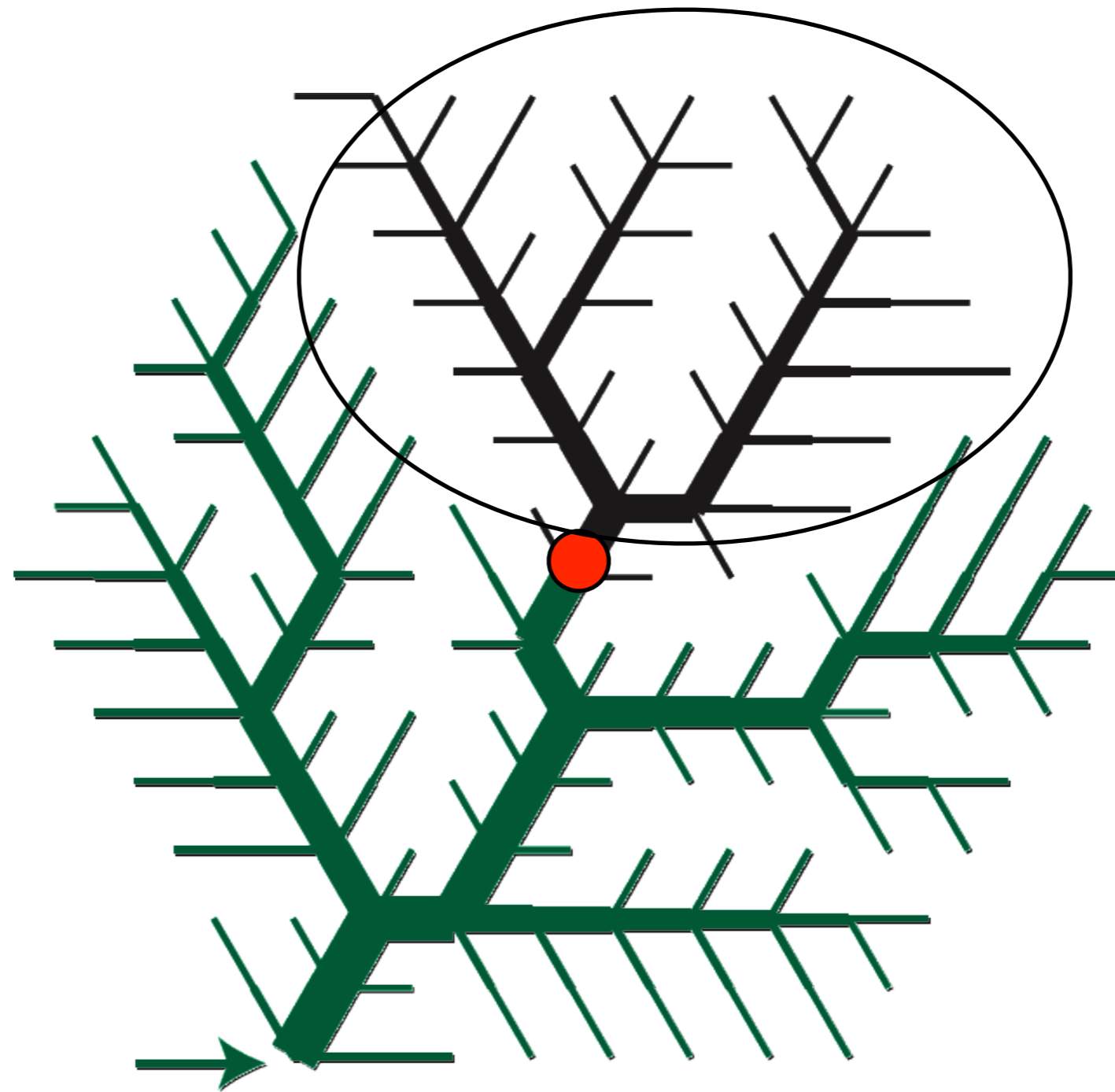


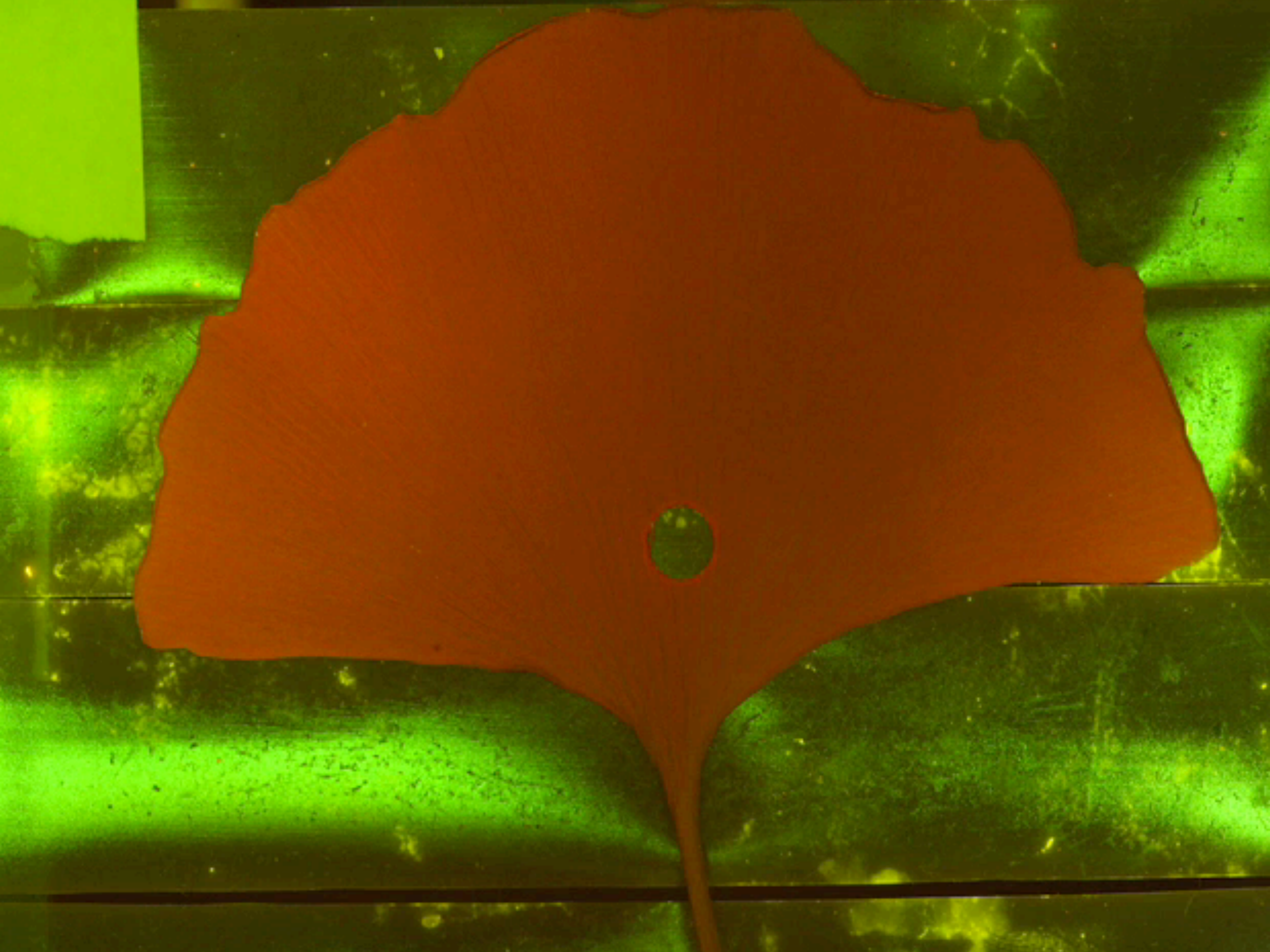
Hausmania (200 myo)



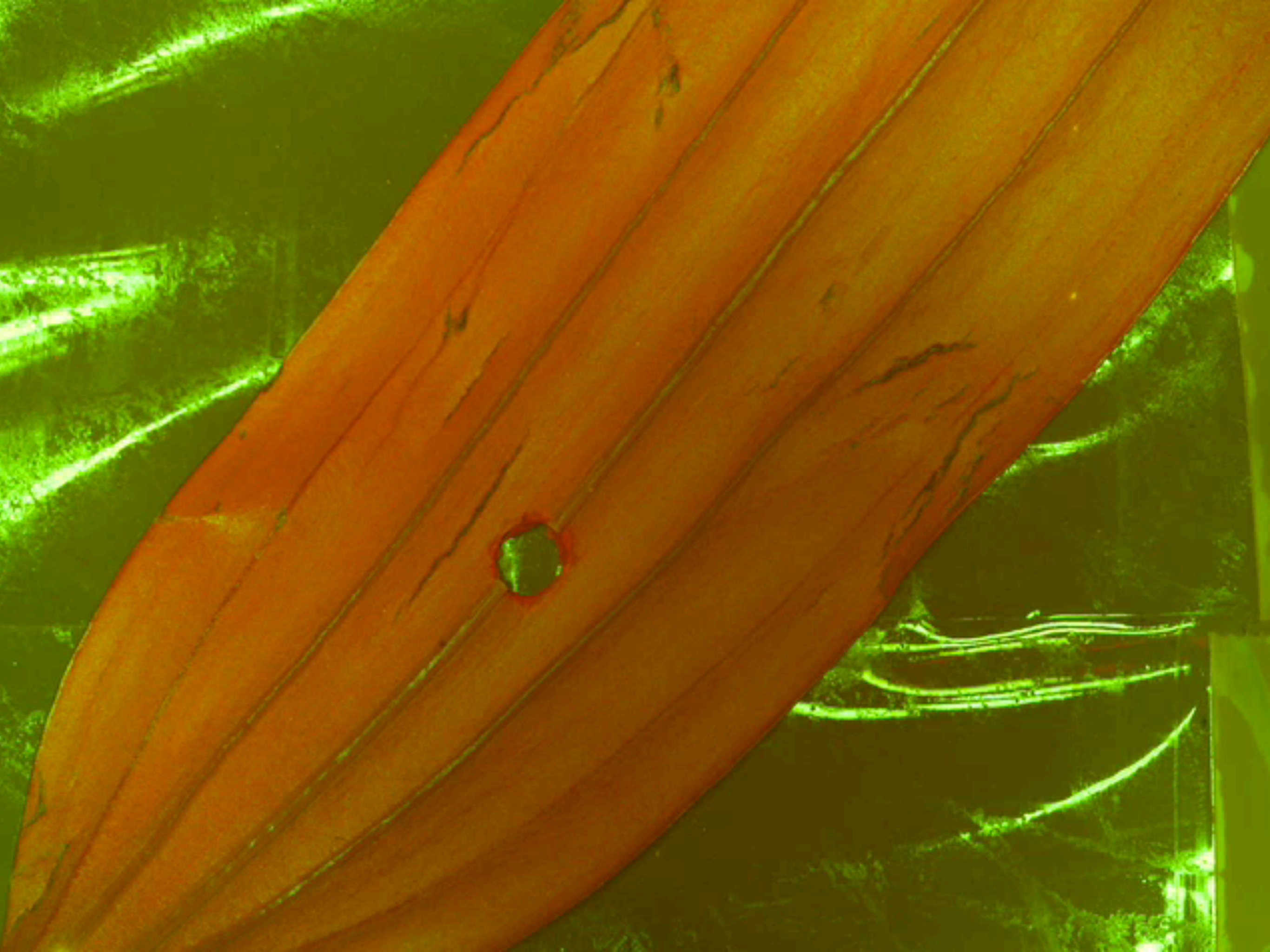
Wang and Zhang (2009)

Loops confer redundancy

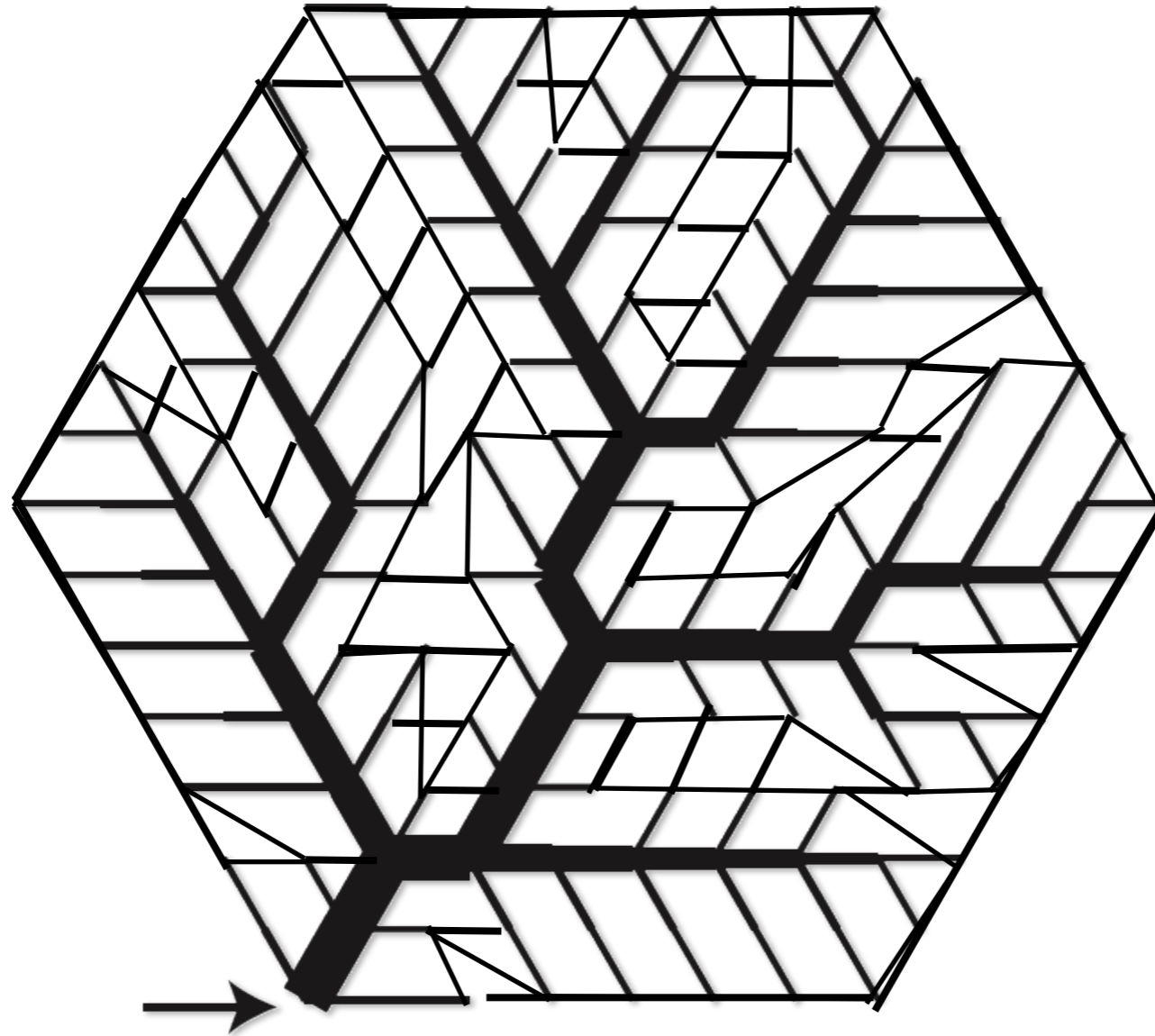








Many ways to confer robustness

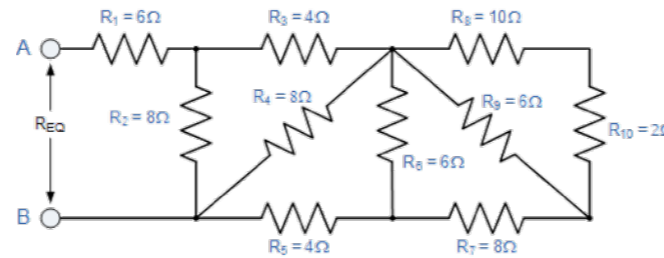


Optimization

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: $V = IR$



Fix the source (net) currents

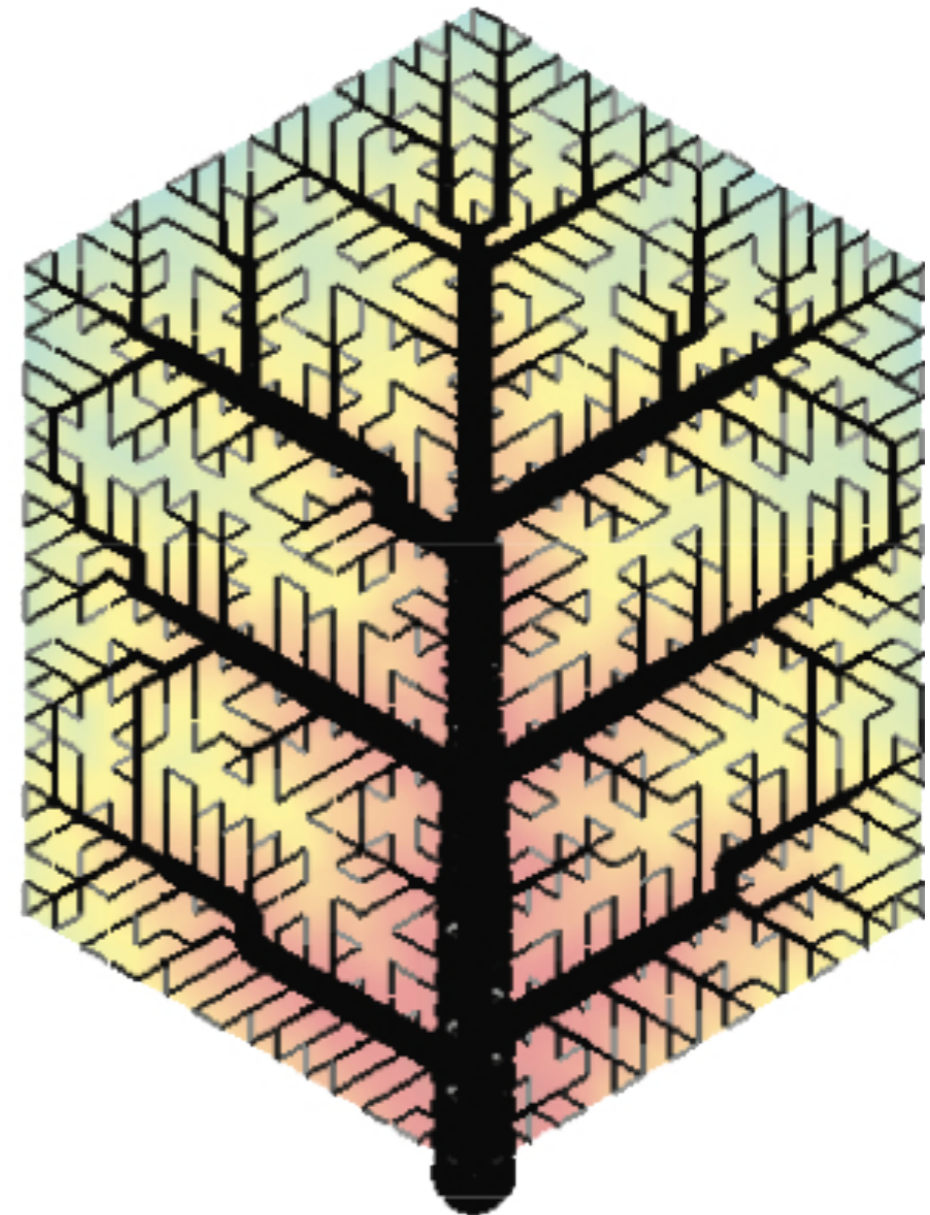


EK et al, PRL 2010

Fix the cost to build network

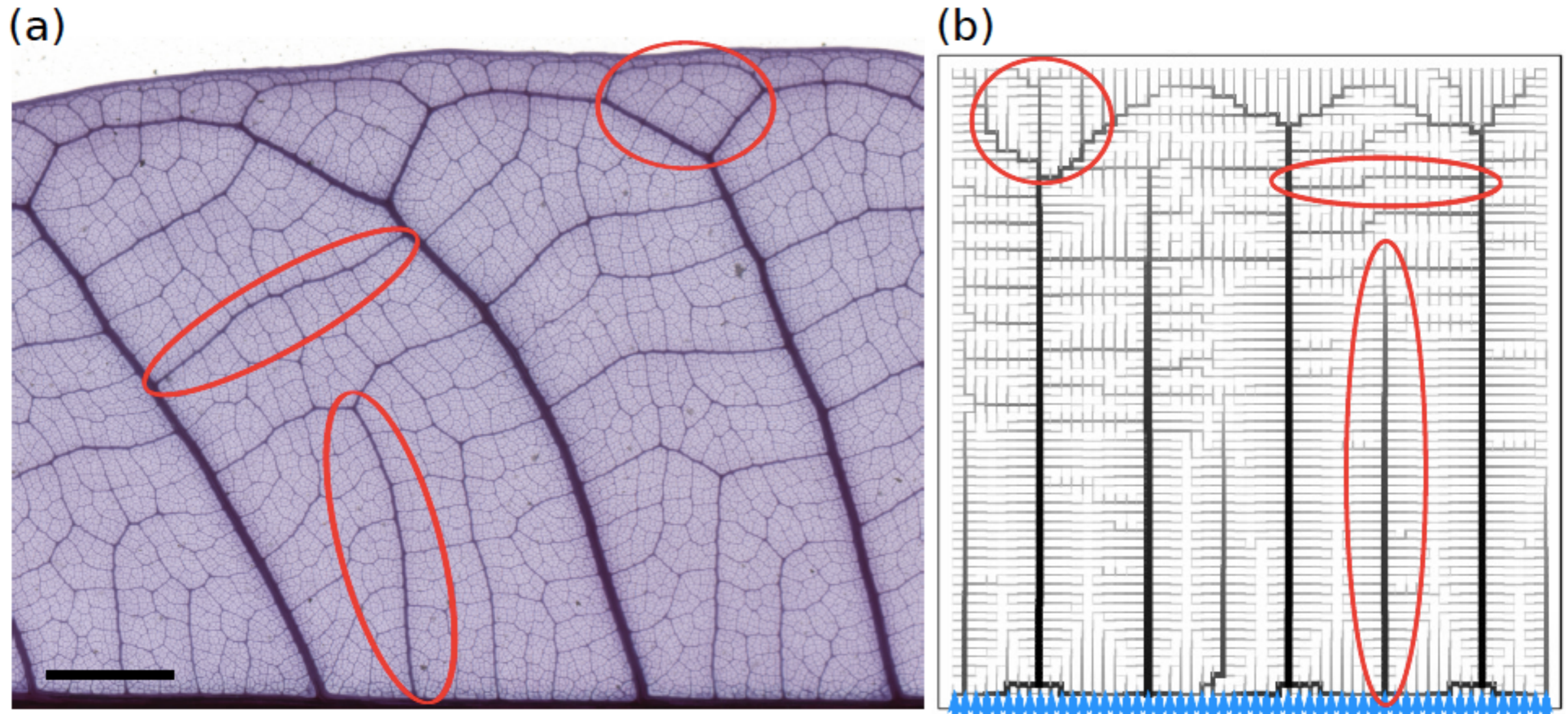


Minimize average water pressure drop



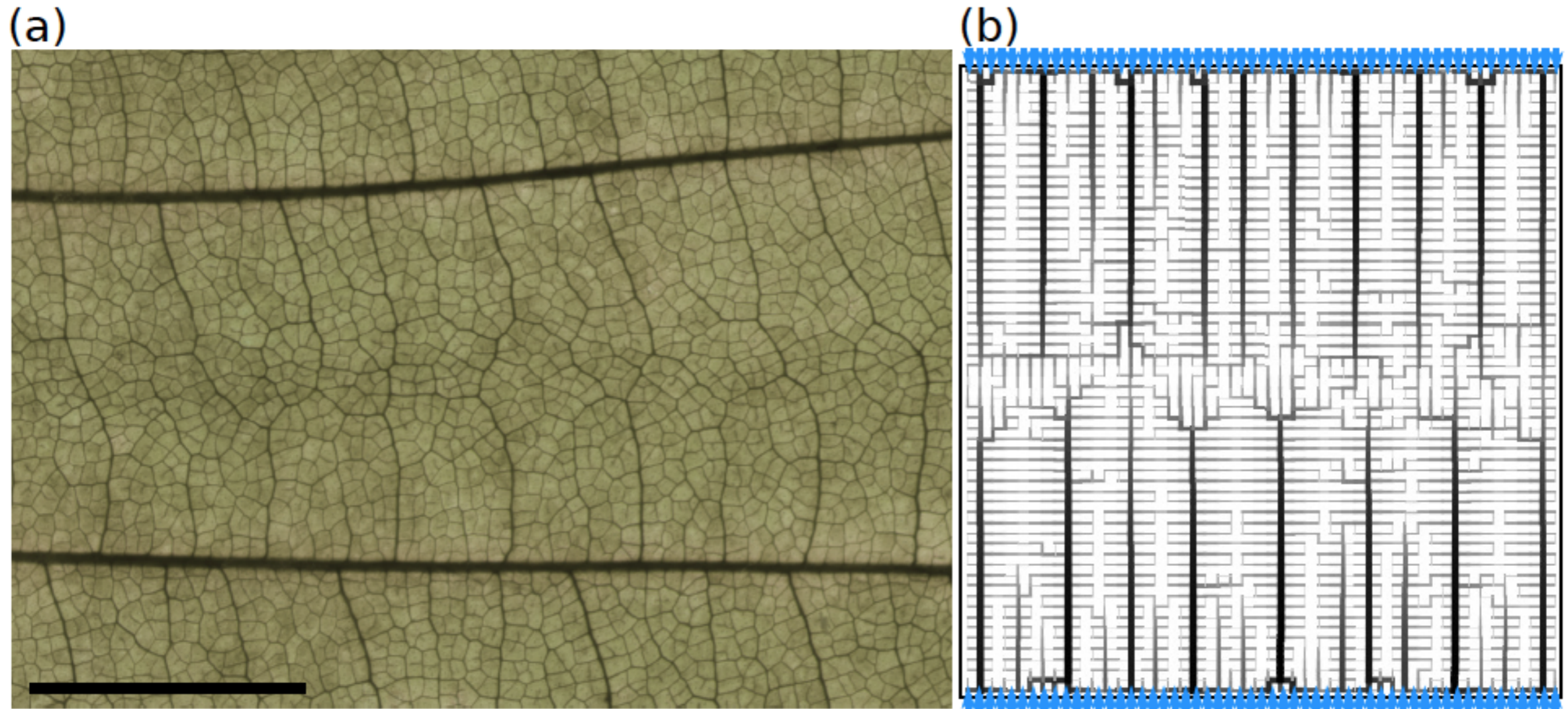
Optimization

Zooming in

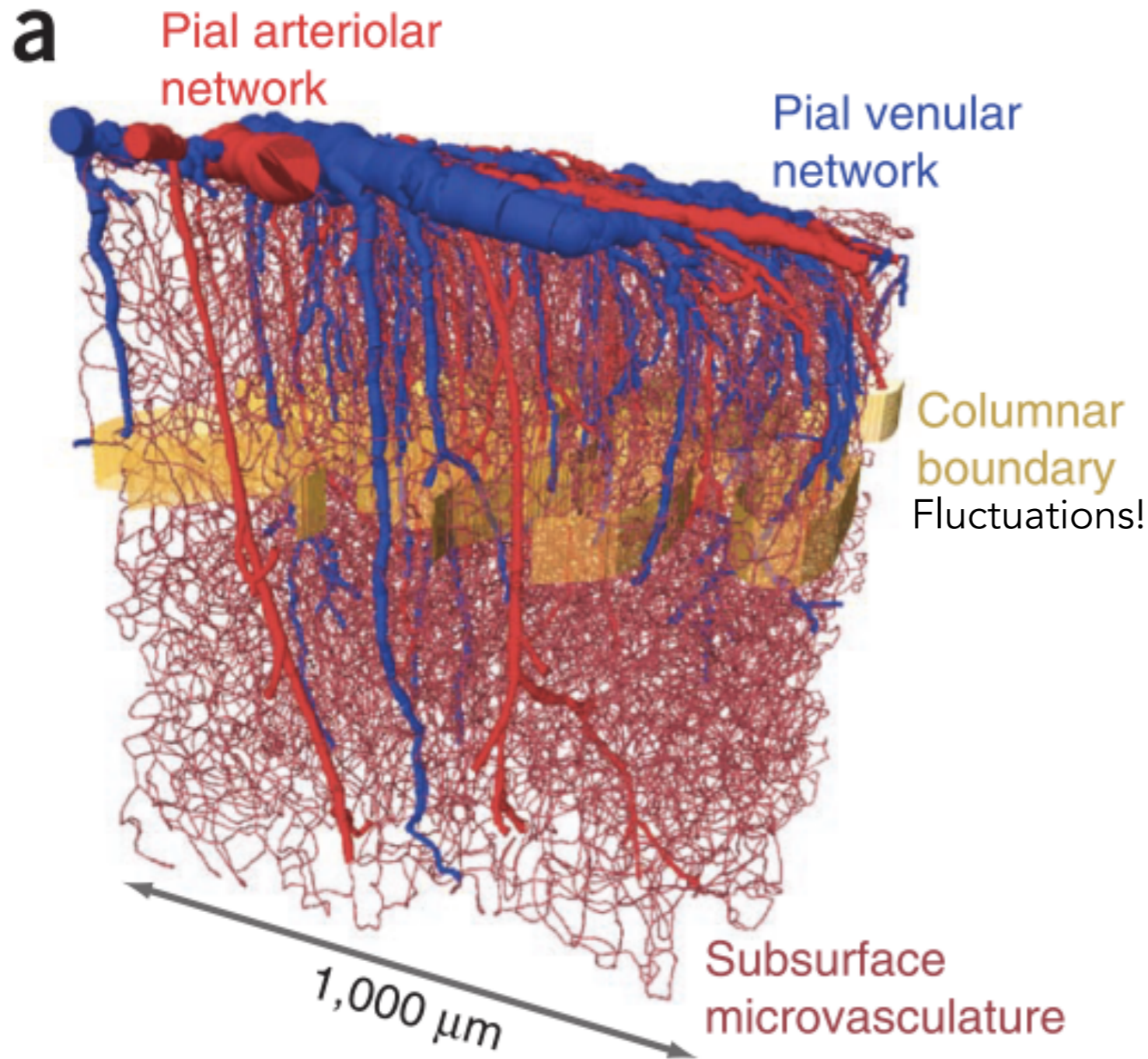


Optimization

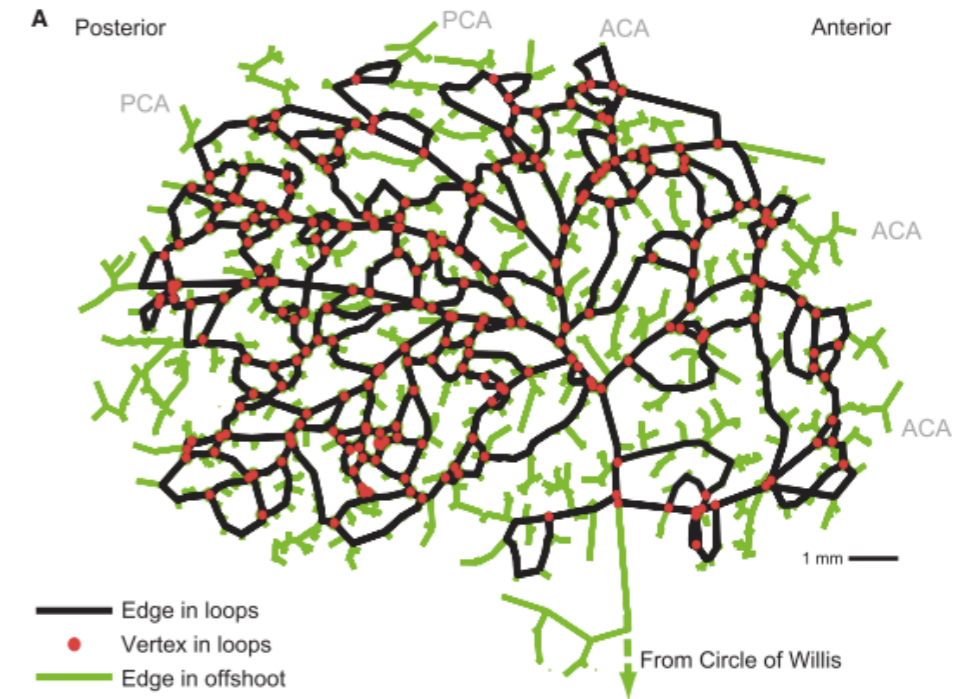
Zooming in even more



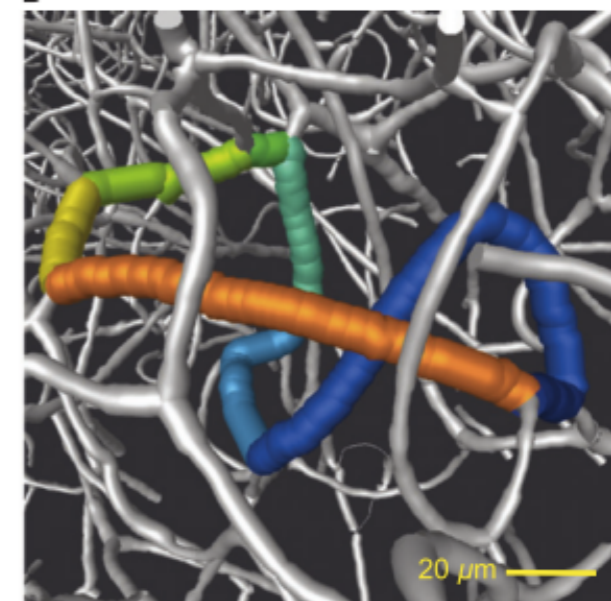
The three tiers of the cortex vasculature



Surface arterial network



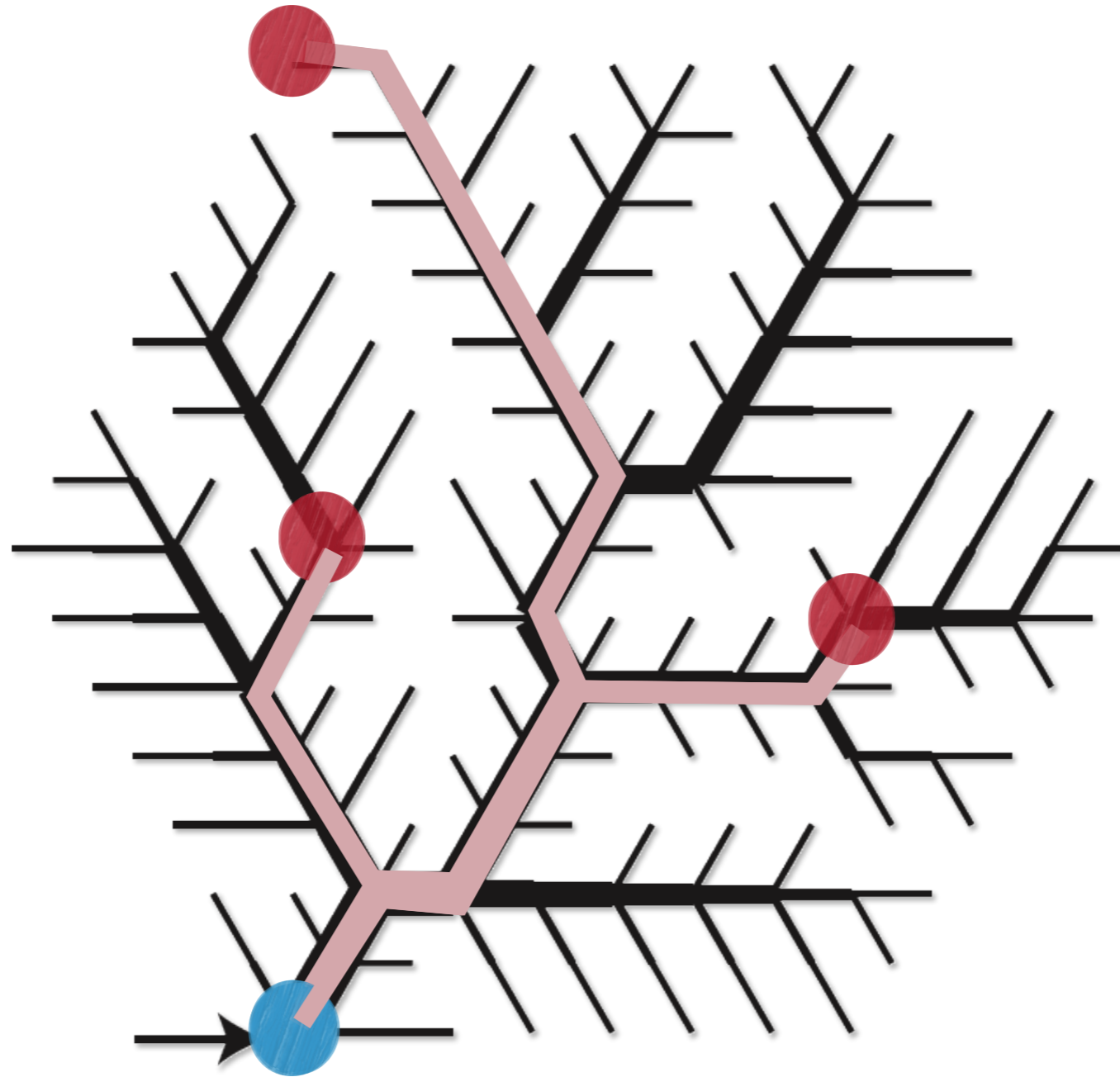
Subsurface microvasculature



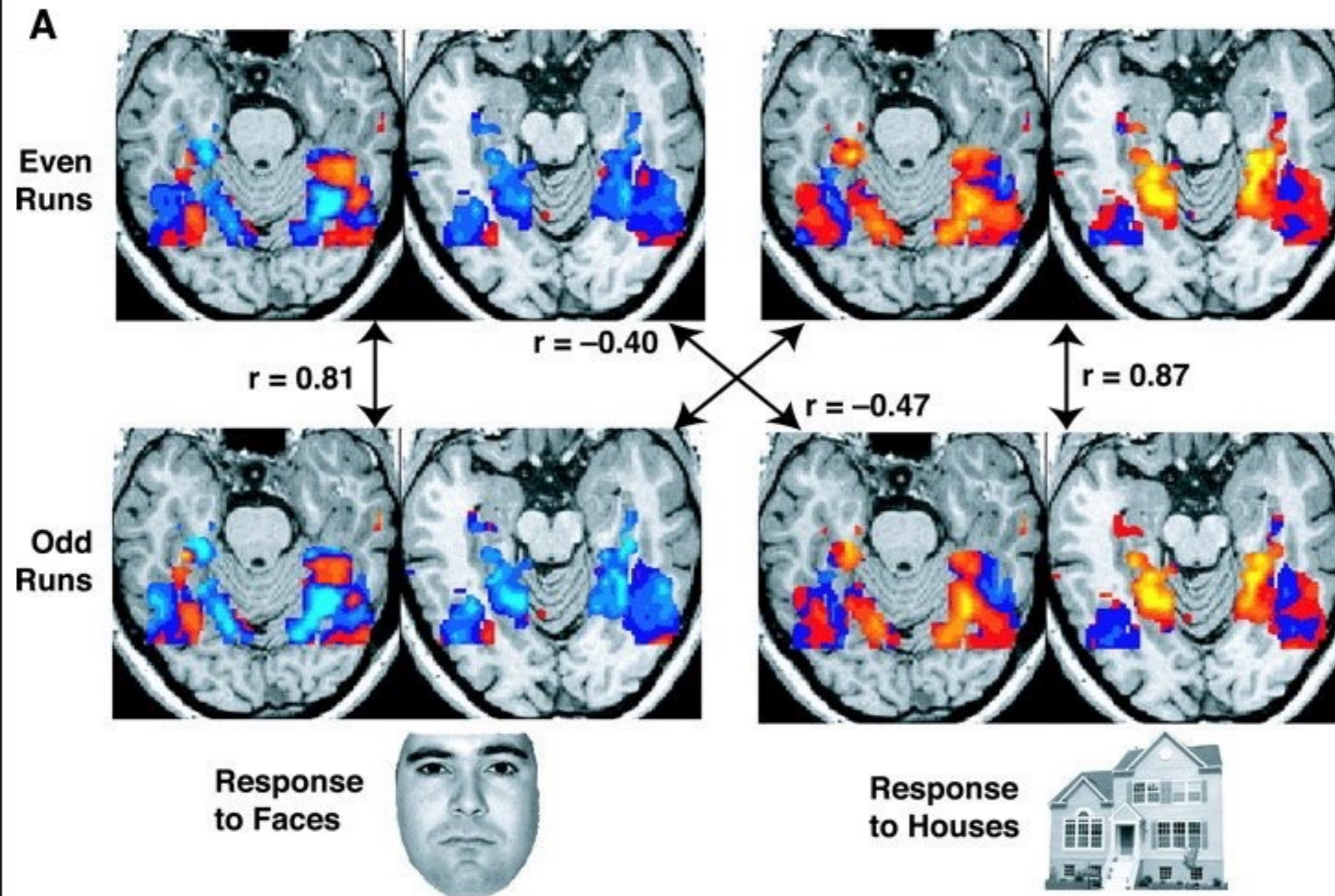
Blinder et al, Nature neuroscience 2013

Shih et al, Microcirculation 2015

Fluctuations

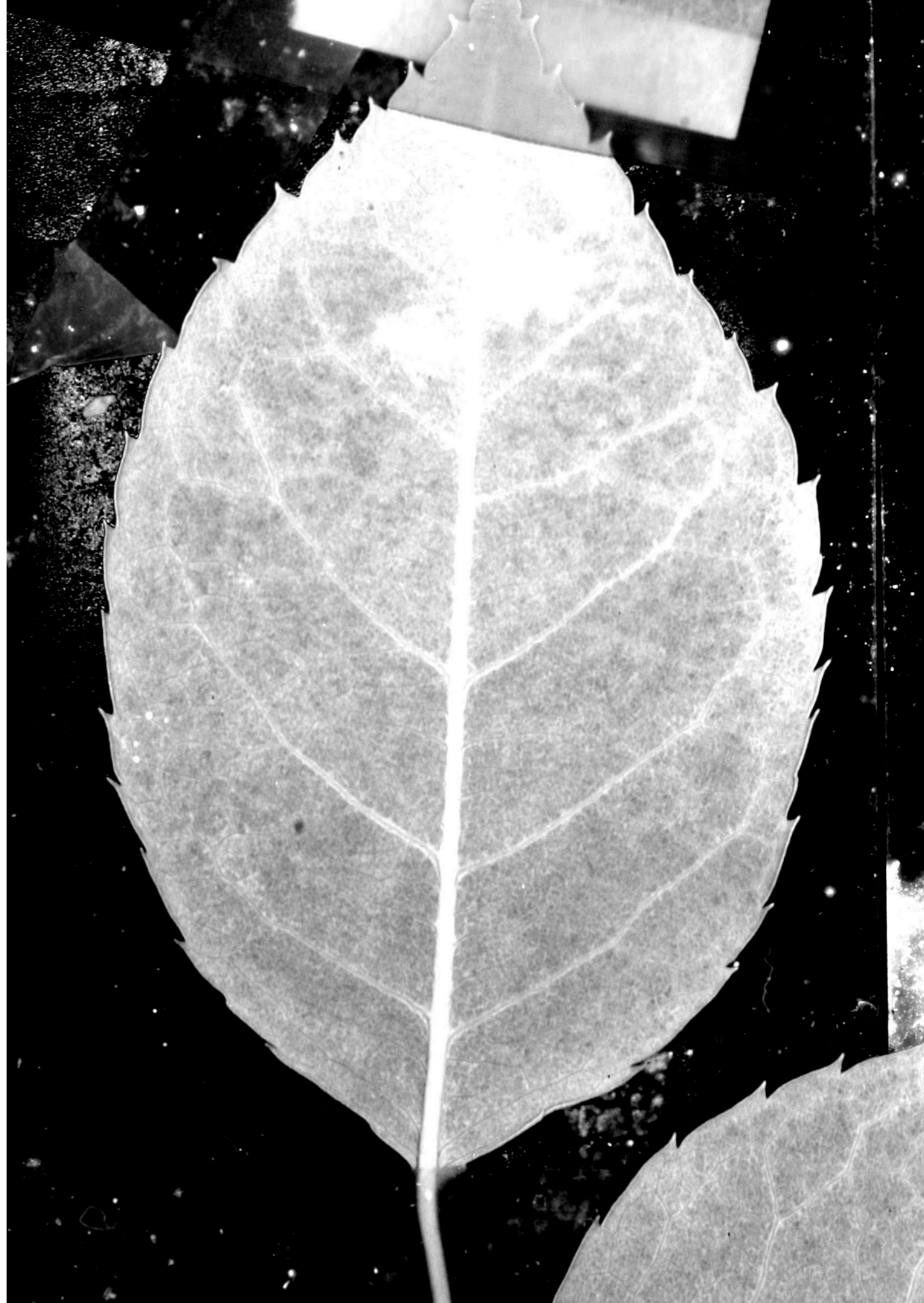
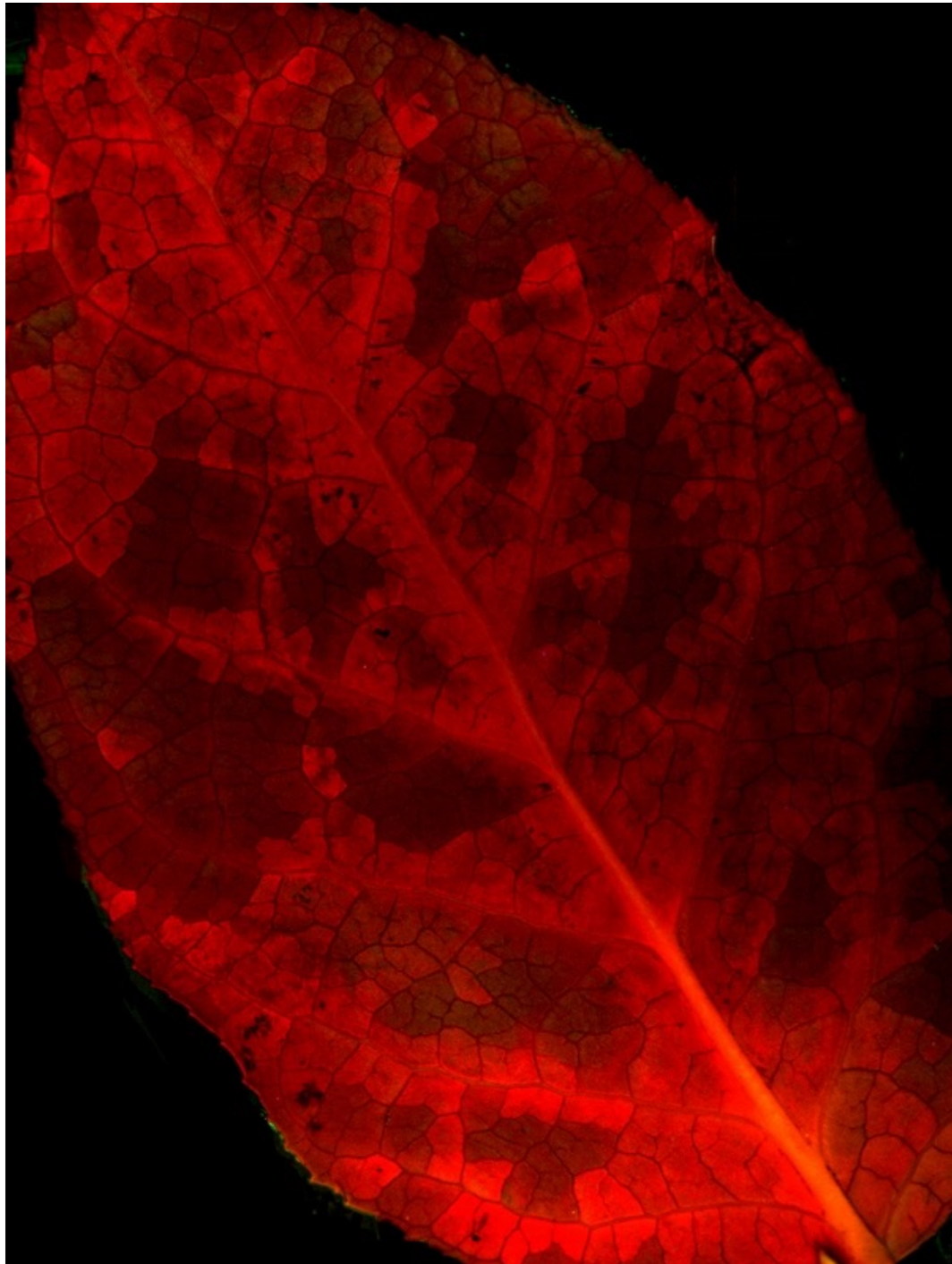


Hemodynamic response of the brain



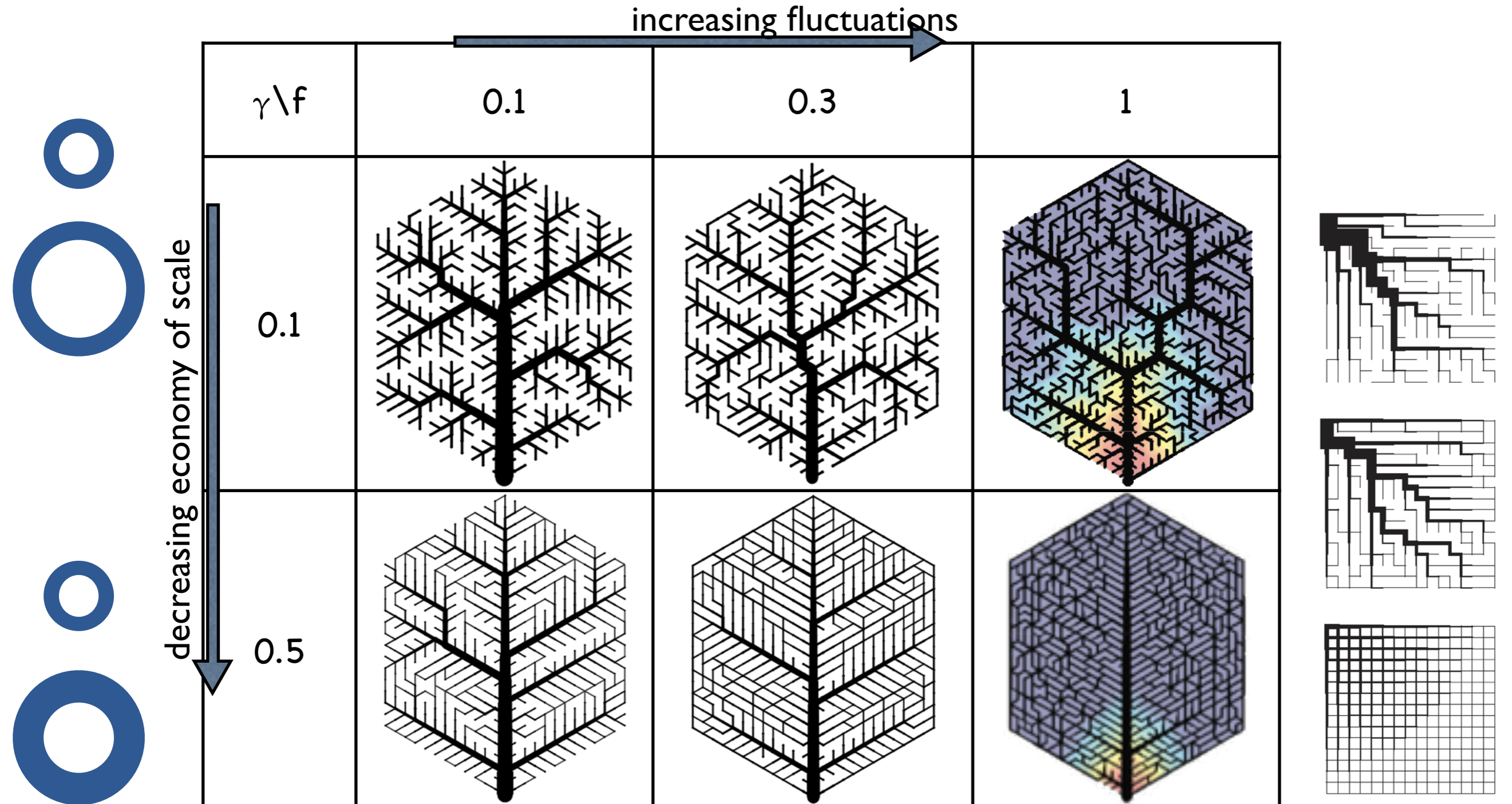
By National Institute of Mental Health - US Department of Health and Human Services:
National Institute of Mental Health, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=17982524>

Fluctuations in the photosynthetic activity of the leaf



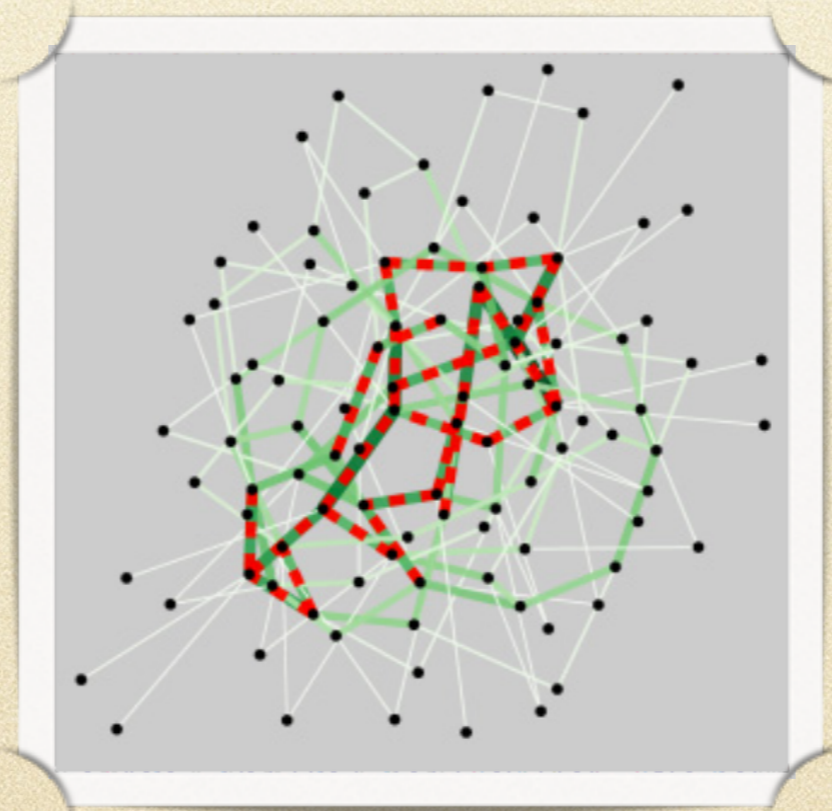
Fluctuations in the load: optimization

net current fluctuations



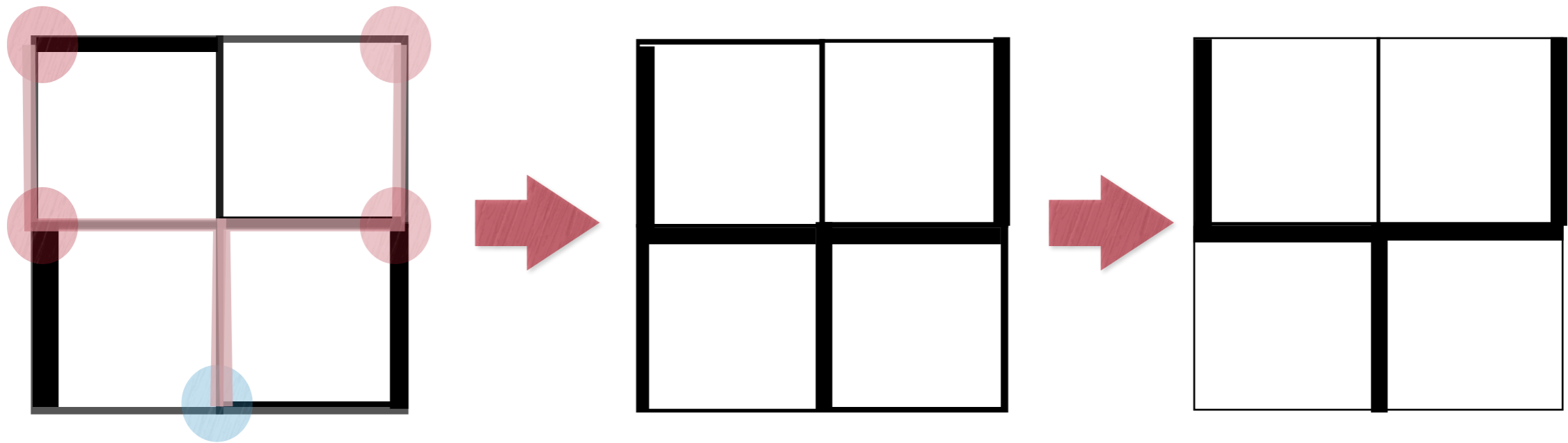
Loops are an efficient way to confer robustness against damage and variability in the load.

**How does nature build an efficient network?
Locally adaptive networks.**

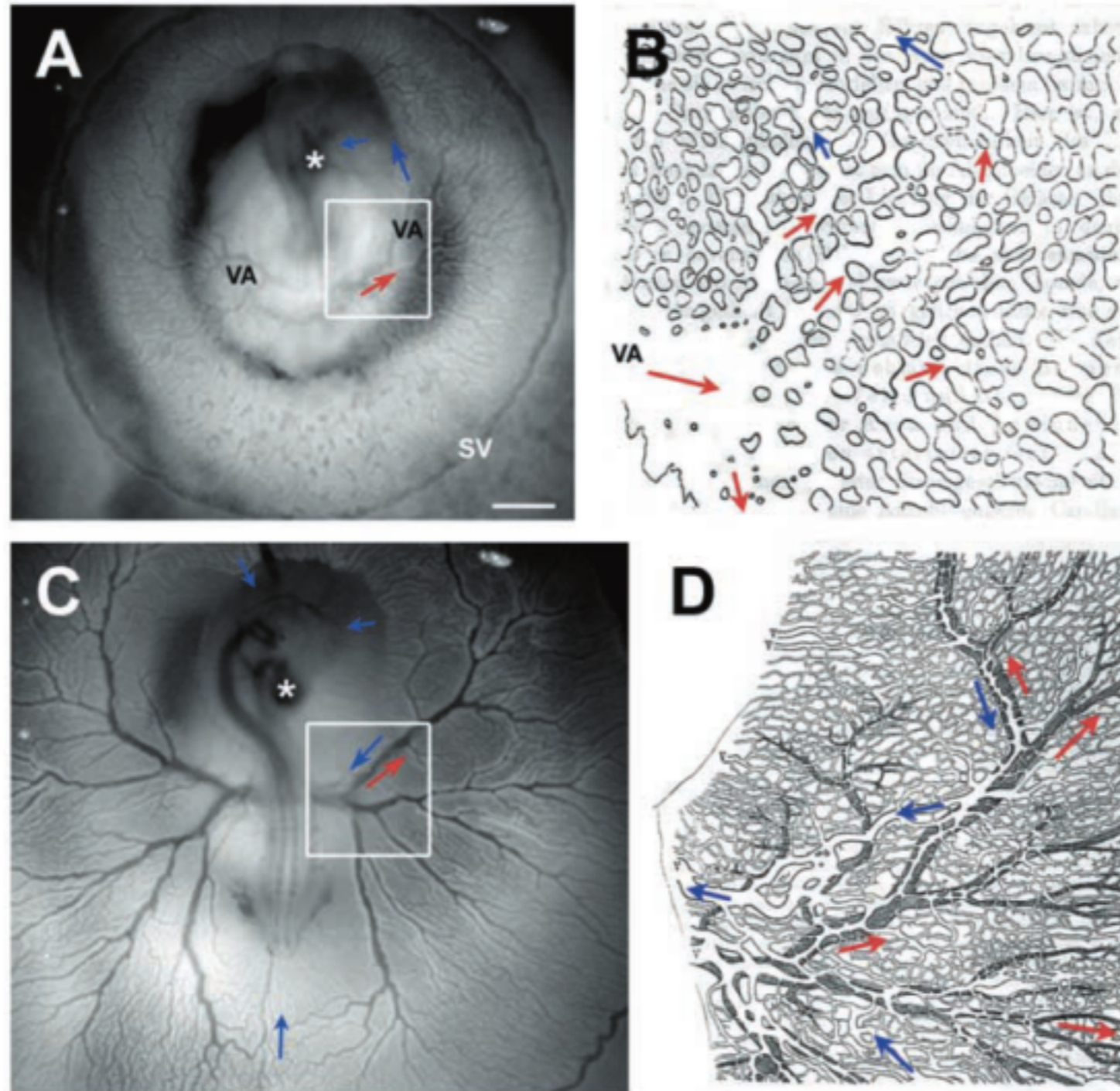


Adaptive networks

Vessels that are used progressively grow,
vessels that are not used gradually disappear



Development



Flow regulates
arterial-venous
differentiation in the
chick embryo
yolk sac

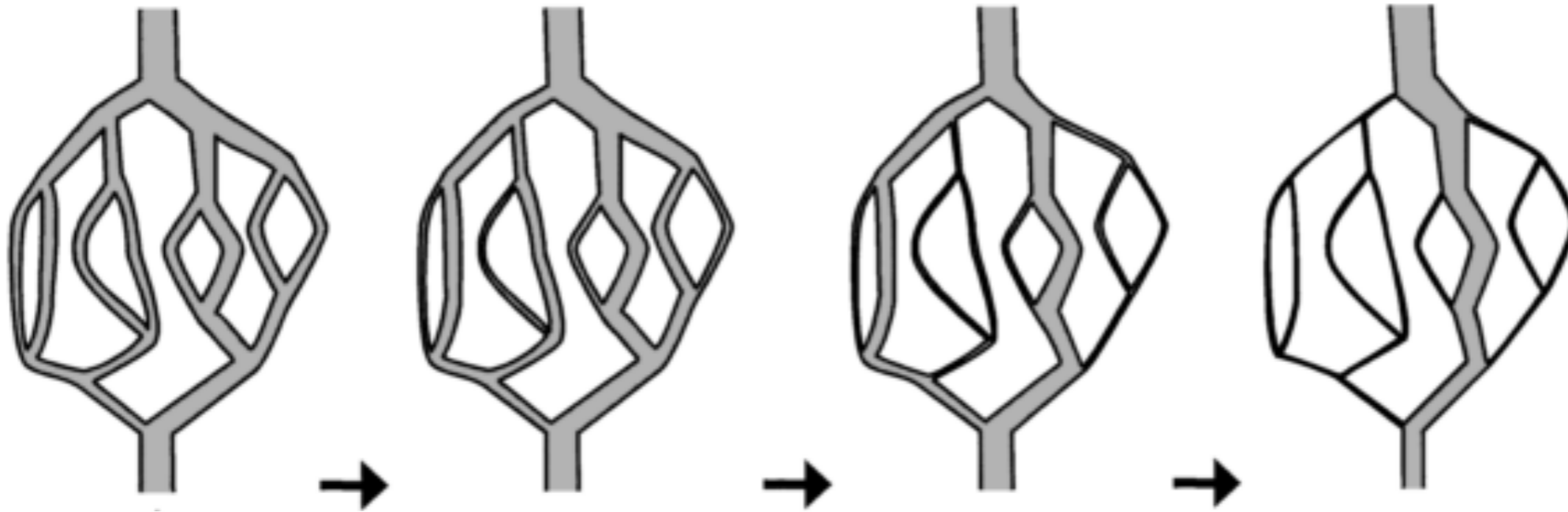
Fig. 1. Overview of arterial-venous differentiation in the yolk sac. (A) Yolk sac vessels just after the onset of perfusion. The vitelline artery (VA) is just beginning to form. Direction of arterial and venous blood flow is indicated by red and blue arrows respectively. The heart is indicated (*). (B) 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

wall shear stress!

Vascular remodeling and adaptation

The importance of fluctuations



Pries et al, AJ Physiology, 1998

The problem of vascular shunting

Fluctuations stabilize vascular structures! No need for metabolic signaling to avoid shunting

Hu et al, PLoS ONE, 2012

A simple adaptive model

Adaptive networks

$$I = \Delta p / R$$

$$Q_{ij}^{kl} = \frac{C_{ij}}{l_{ij}} \cdot (p_i^{kl} - p_j^{kl})$$

Average current

$$\langle |Q_{ij}| \rangle := \frac{1}{\frac{N \cdot (N-1)}{2}} \sum_{(k,l) \in \mathcal{P}} |Q_{ij}^{kl}|$$

Update the conductivity

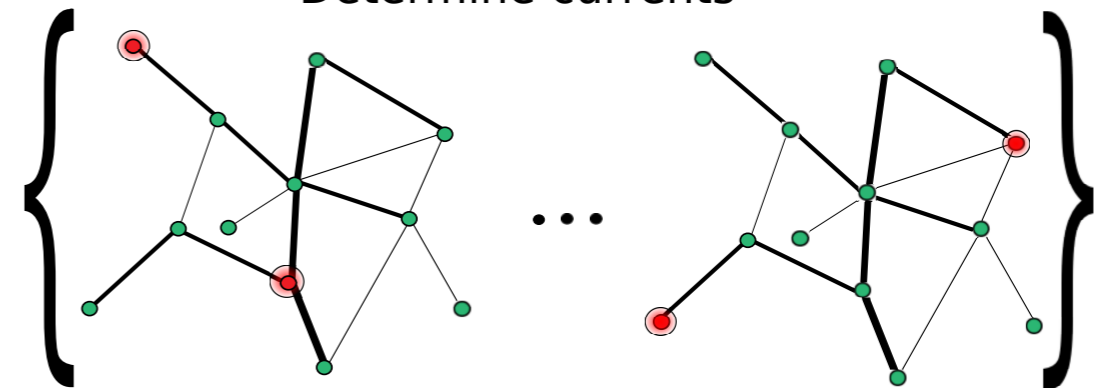
$$\frac{dC_{ij}(t)}{dt} = \beta \cdot f\left(\frac{\langle |Q_{ij}(t)| \rangle}{\epsilon}\right) - \alpha \cdot C_{ij}(t)$$

Local positive feedback

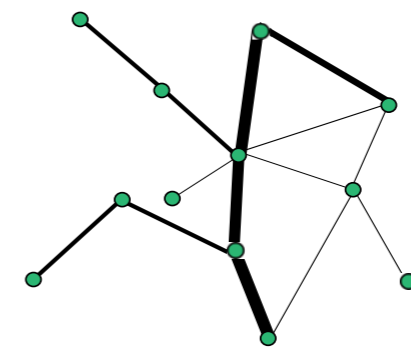
decay term

Update model

Determine currents



Update link weights

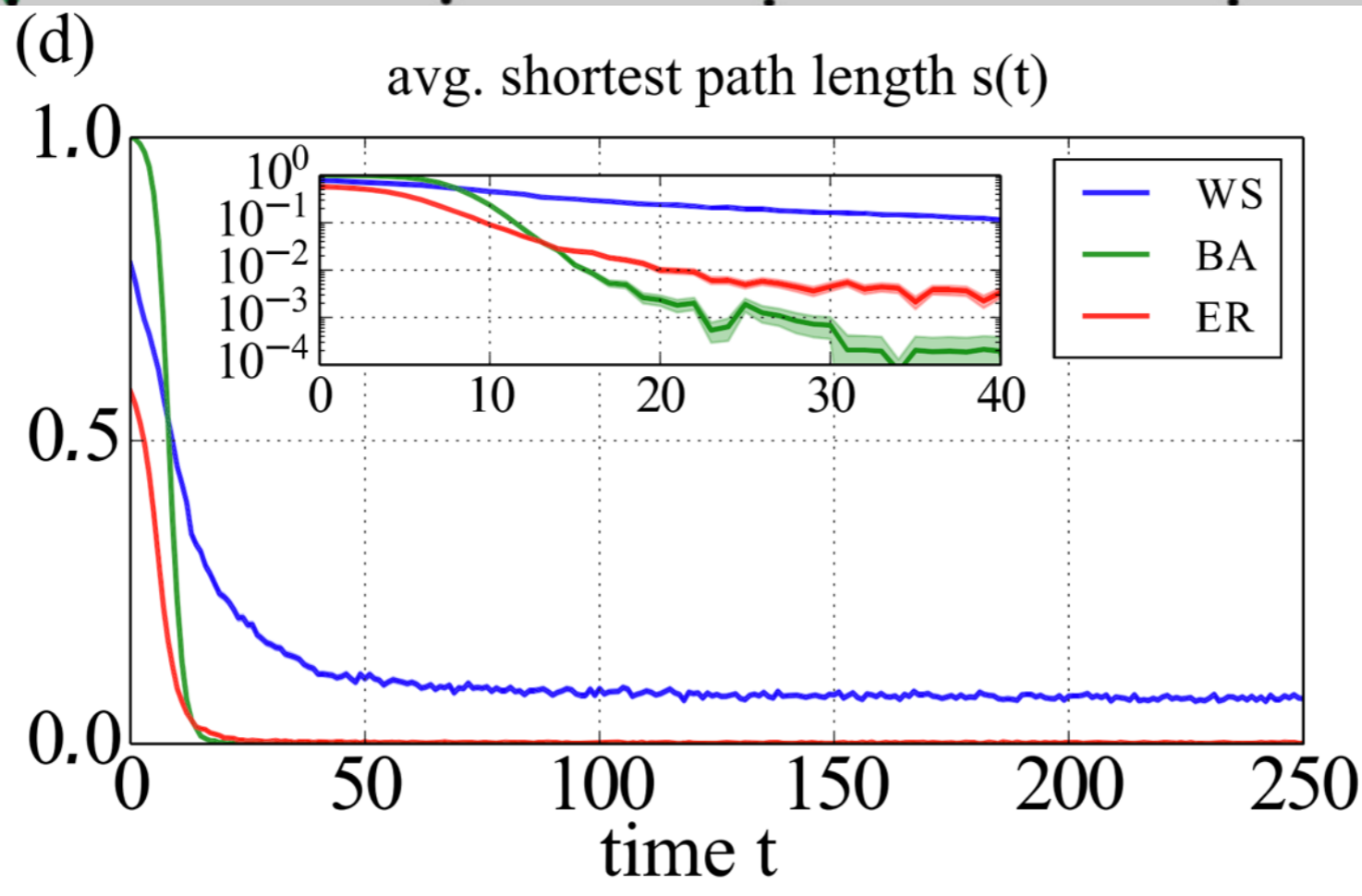
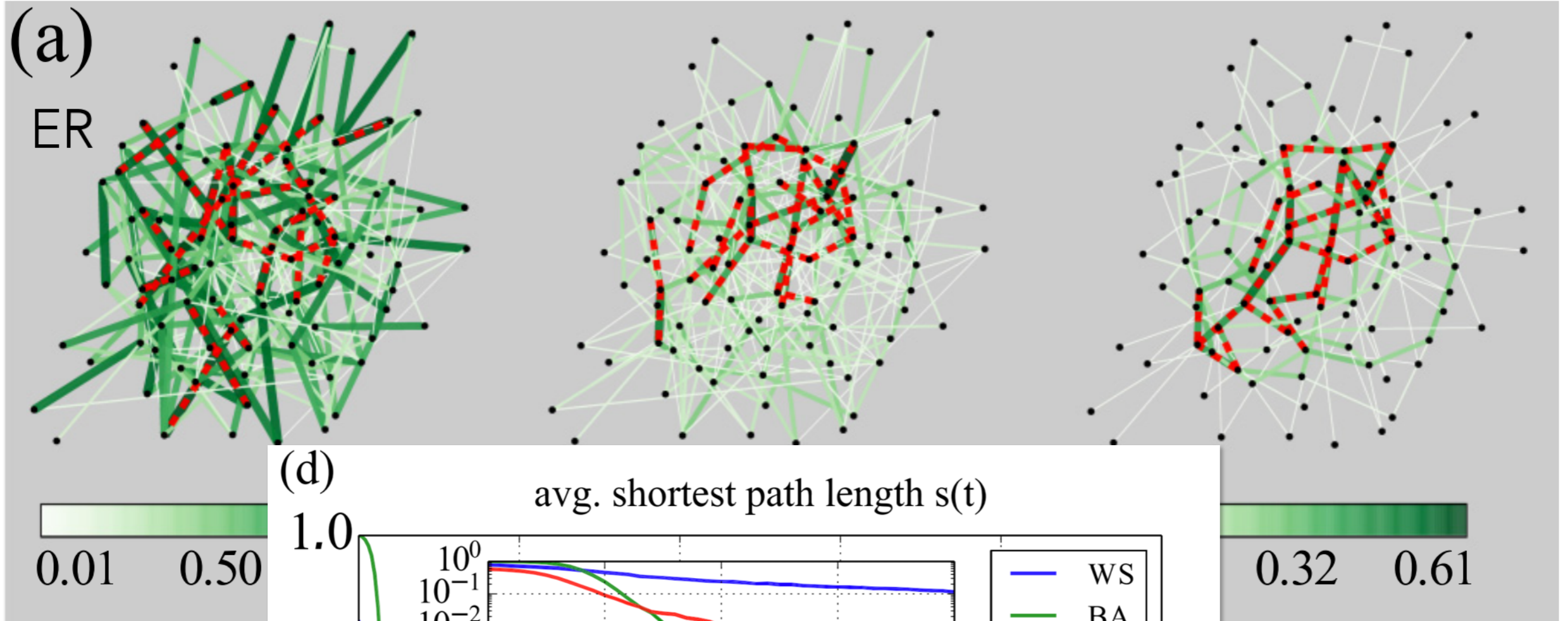


Adaptive networks

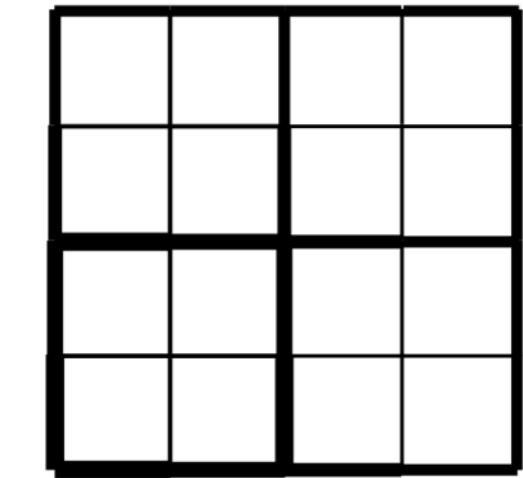
time $t = 0$

time $t = 5$

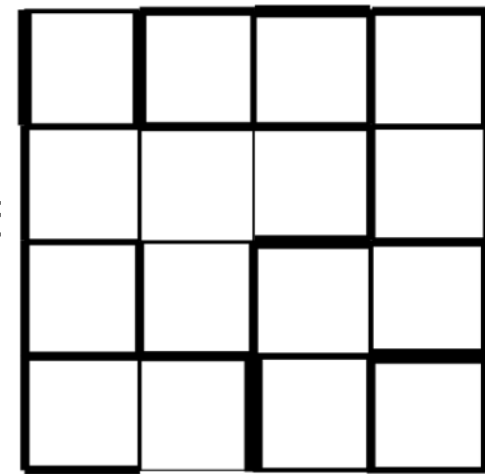
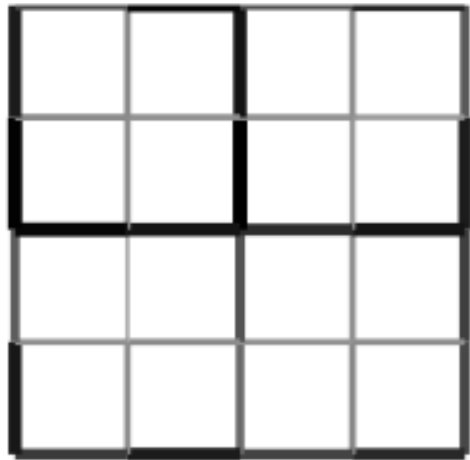
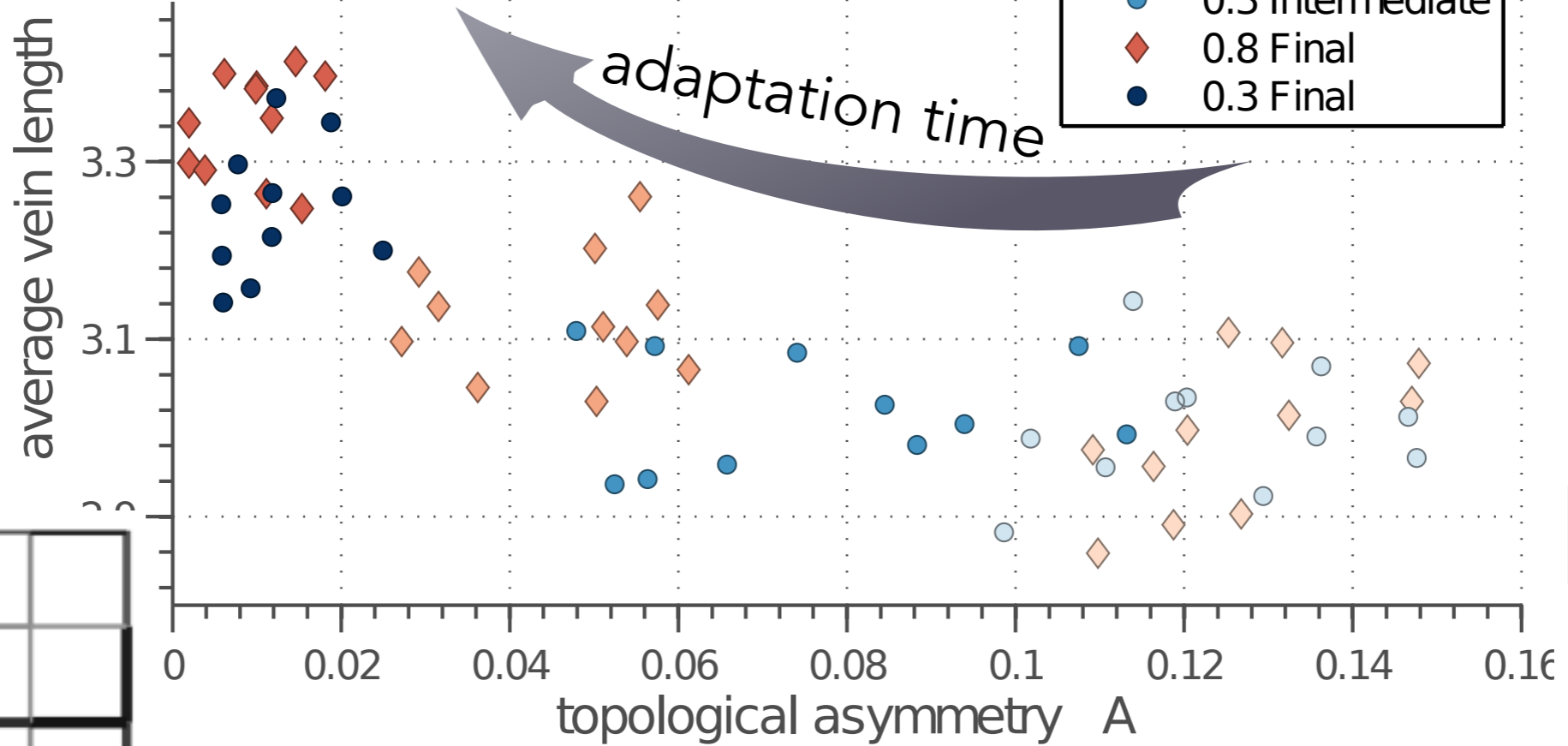
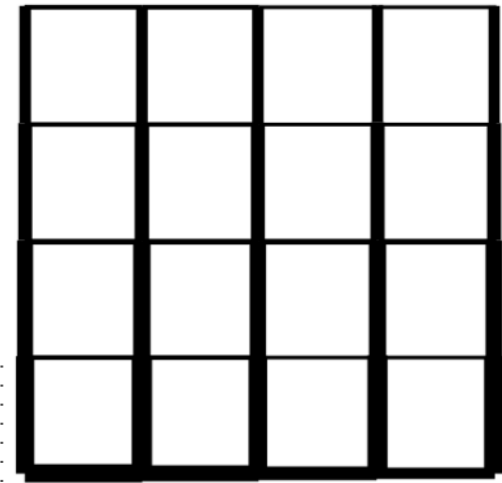
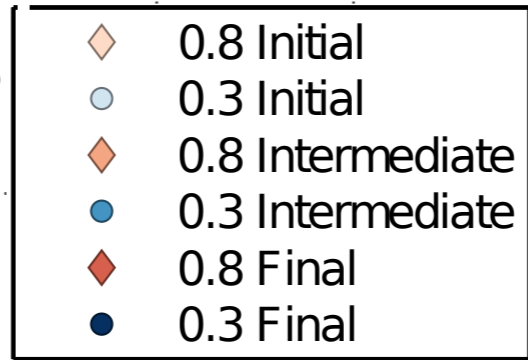
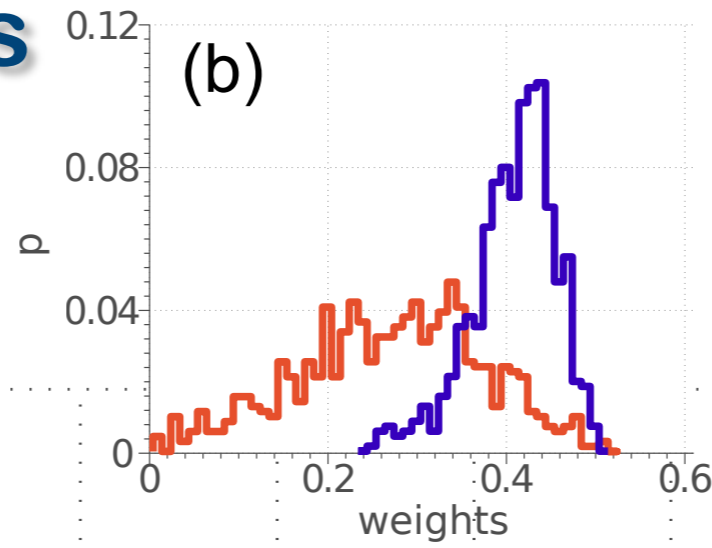
time $t = 1000$



Adaptive networks



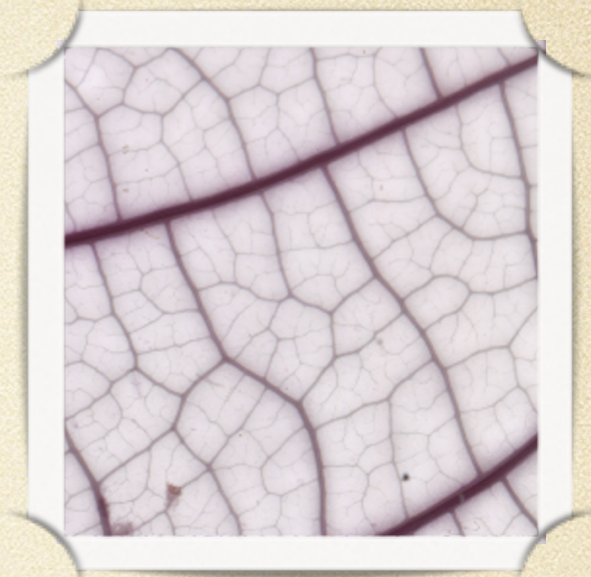
(a)



Summary

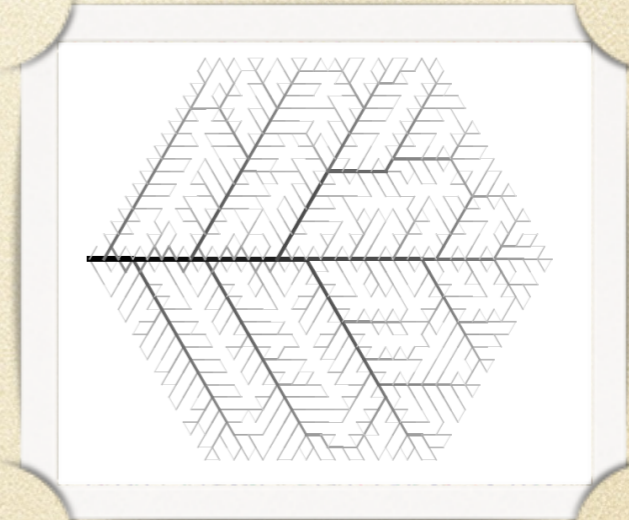
"What"

Loops and hierarchical nestedness are ubiquitous in biological networks



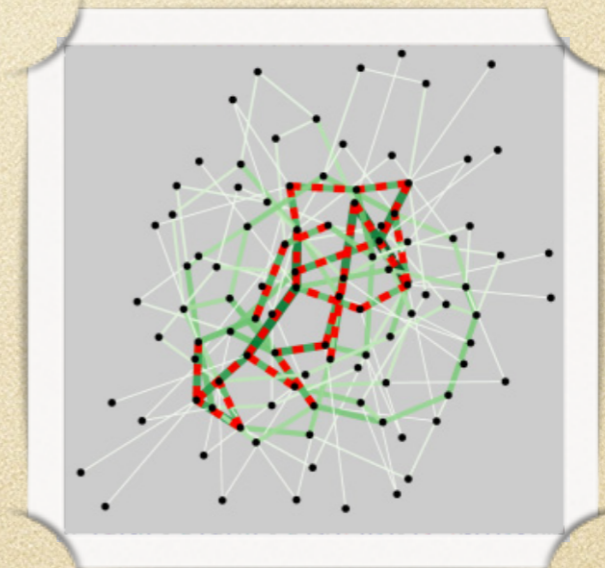
"Why"

Optimality principles: Loops are optimal for robustness and fluctuations



How

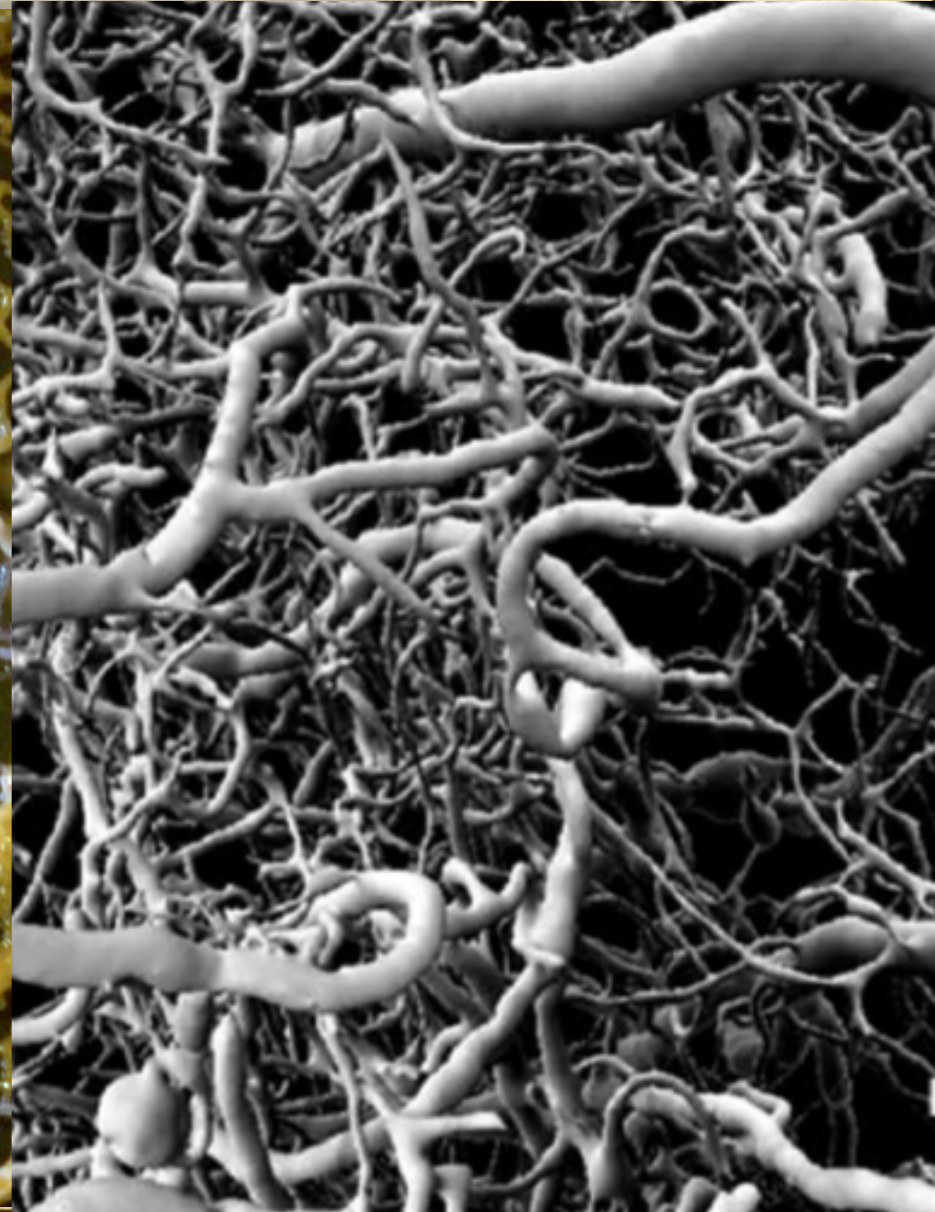
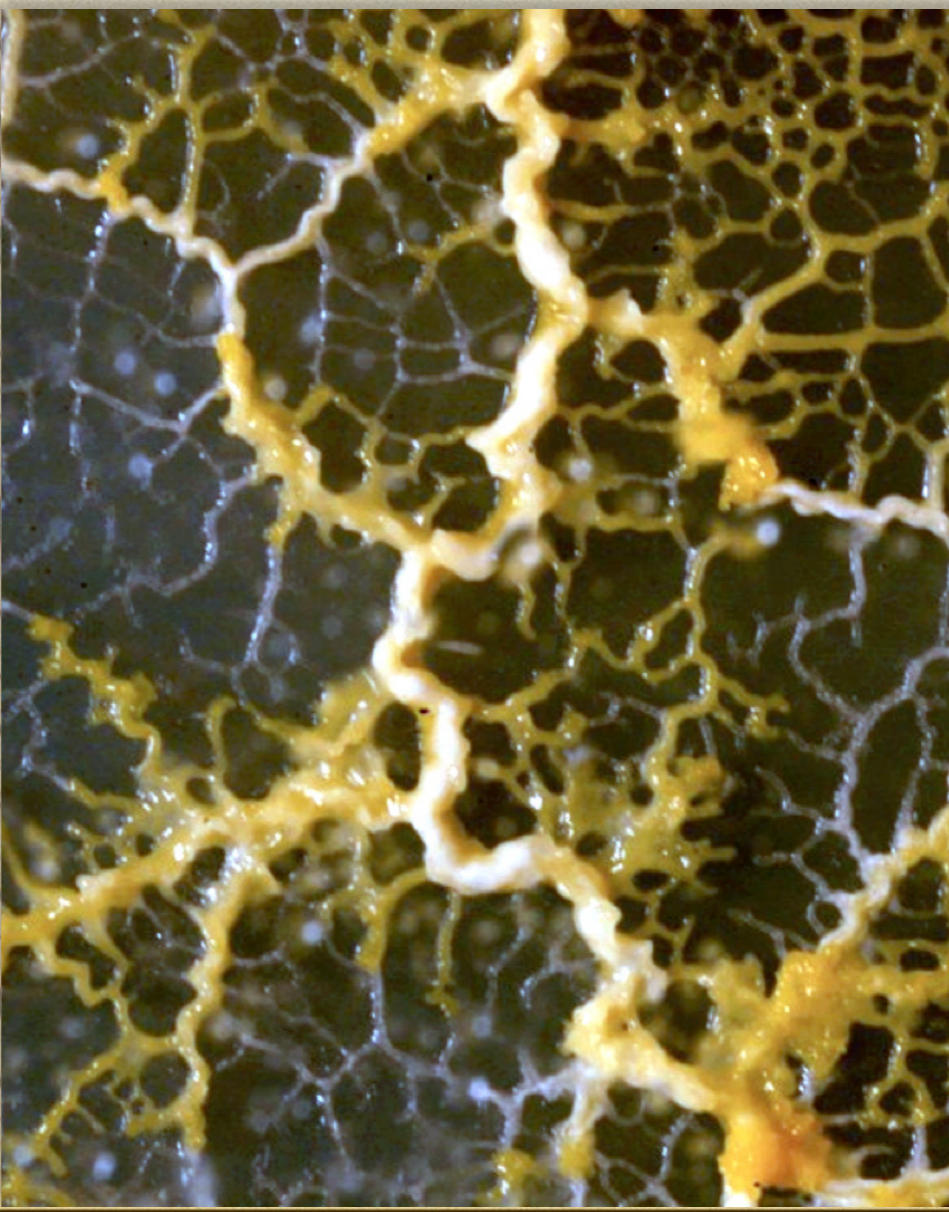
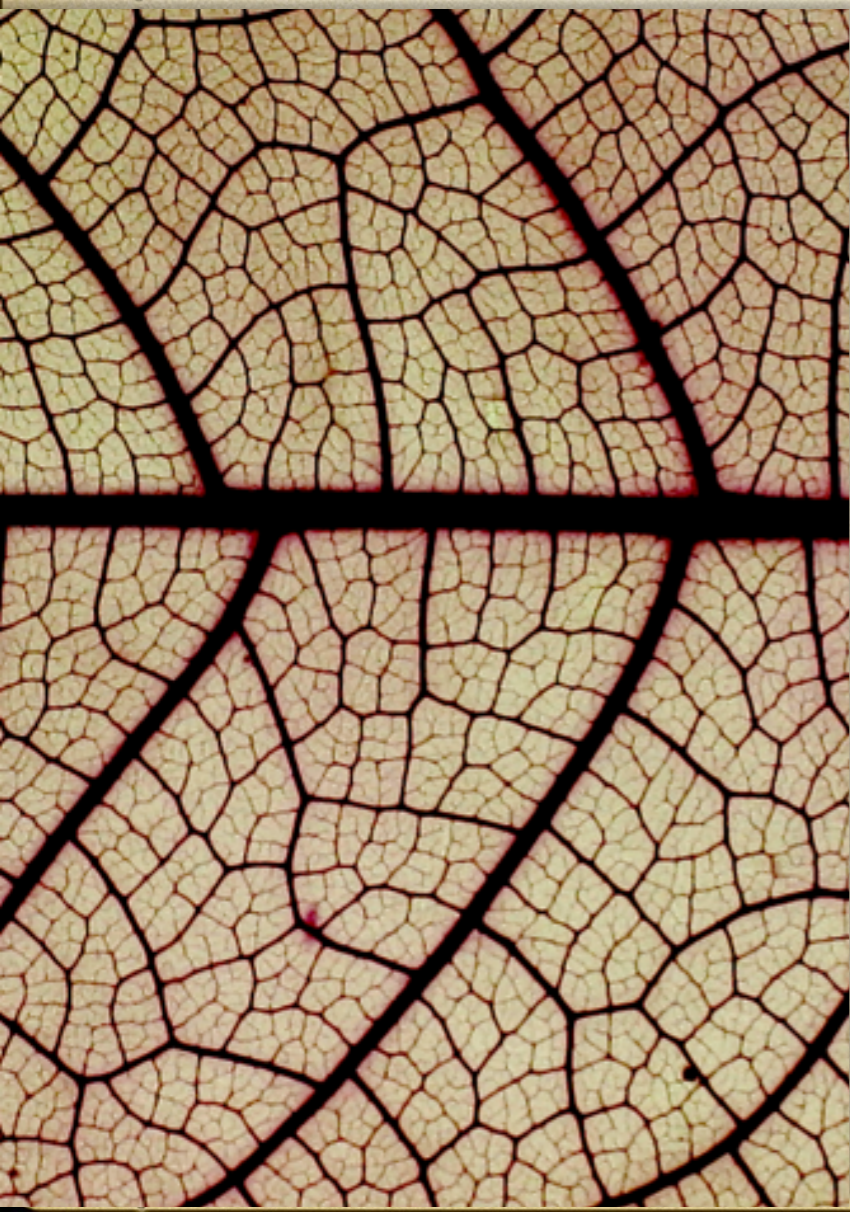
Locally adaptive rules create loopy hierarchically nested graphs



Towards universal principles

Plants, slime molds, our own venation

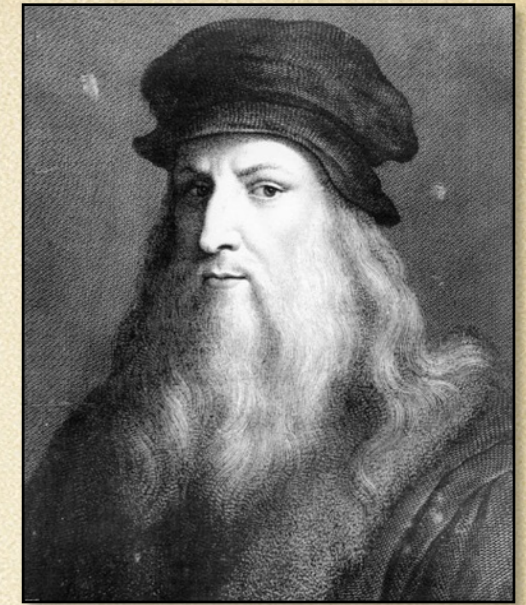
Hierarchical, full of nested loops: common principles, but also differences in the architecture. What are the differences, and what can they tell us about the function?



“The veins of the water”

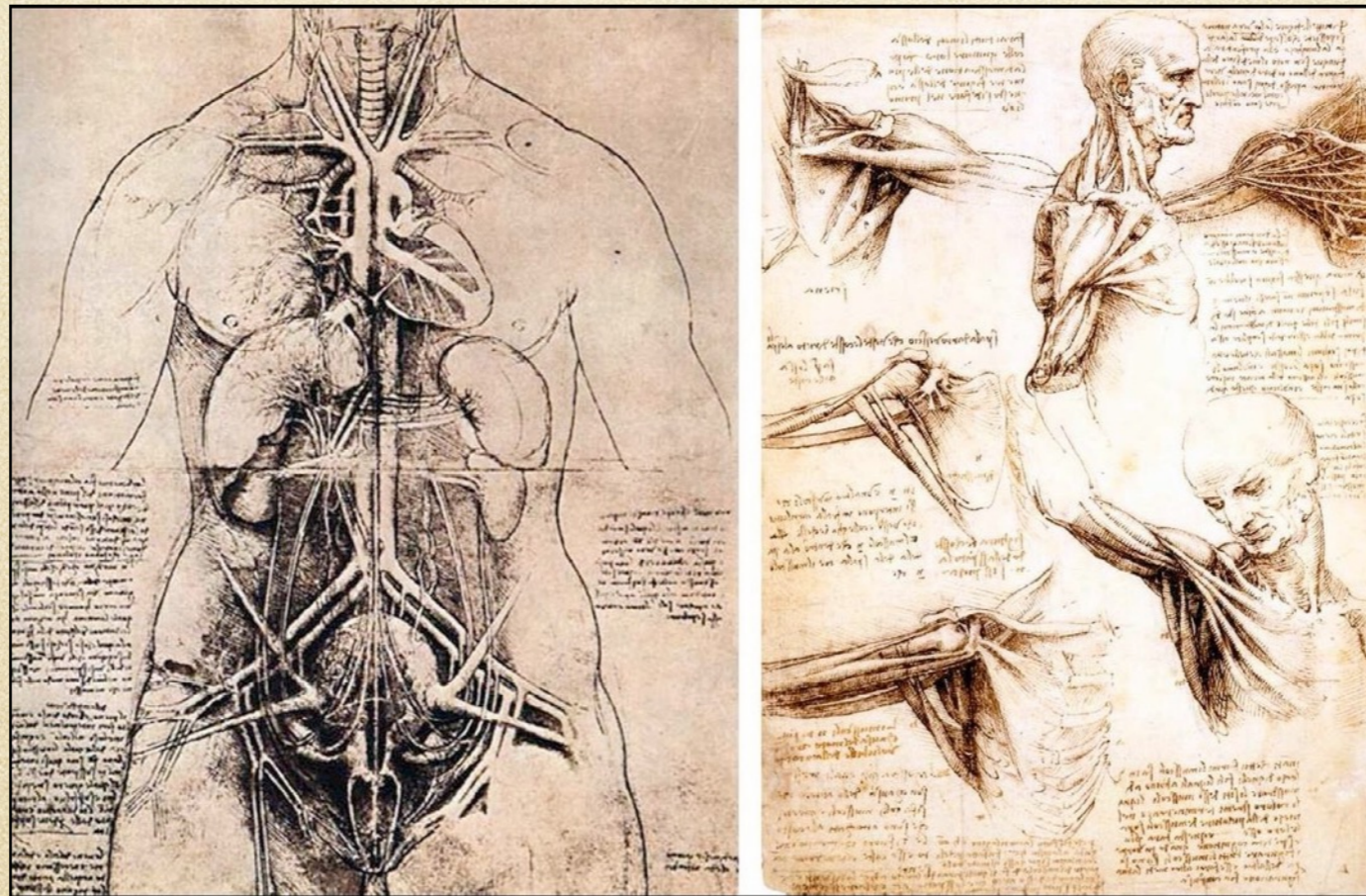
The earth and the human body are both governed by the same physical laws, and for this reason rivers and veins share common architectural principles.

The idea appeals to me that the earth is governed by nature and is much like the system of our own bodies in which there are both veins (vessels for blood) and arteries (vessels for air). In the earth there are some routes though which water runs, some through which air passes. And nature fashions these routes so like the human body that our ancestors call them “veins of water”.



Leonardo da Vinci
1452-1519

"[The earth]'s blood [is] the veins of the waters."



Students and post-docs

Jana Lasser
Henrik Ronellenfitch
Desislava Todorova
Jonathan Dawson
Johannes Gräwer

Collaborators

Carl Modes
Marcelo Magnasco
Kaare Jensen
Douglas Daly



Funding



Thank you!

