How does a physicist become a biologist?

by
Van Savage
Department of Ecology and Evolutionary Biology
Department of Biomathematics
Quantitative and Computational Biology Institute
UCLA

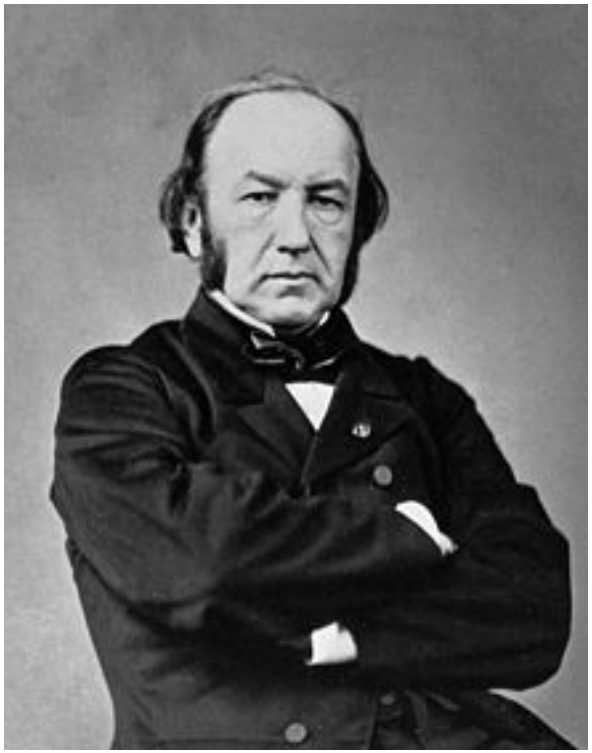
External Faculty
Santa Fe Institute

BernardFest, Wash U, March 26, 2016

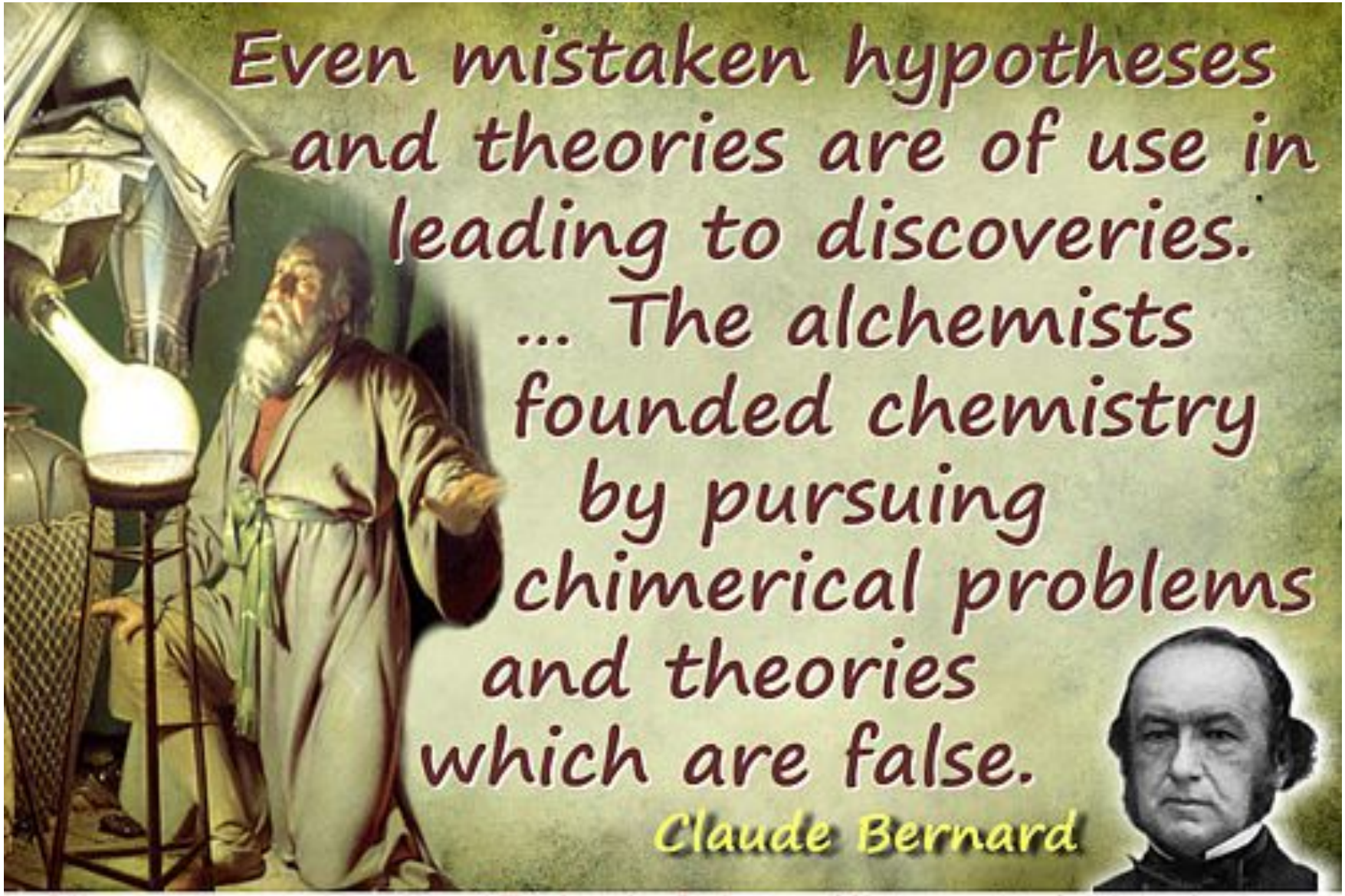
Step 1: Pick the right advisors

Claude Bernard
brilliant physicist

OR



Claude Bernard
father of modern physiology



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Step 2: Borrow some ideas

Energy use and minimization

Fractal space-filling networks

Topology: tree-like or grid-like?

Invariants

Scaling

Finite-size effects

Symmetry and symmetry breaking

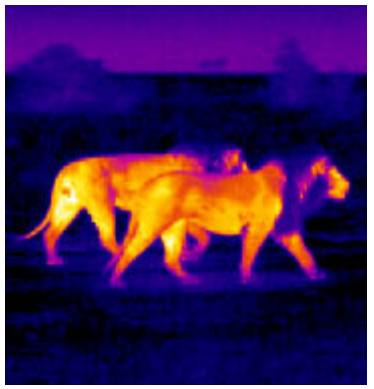
Analyzing big data

metabolic rate—"fire of life"—power for maintenance, growth, and reproduction

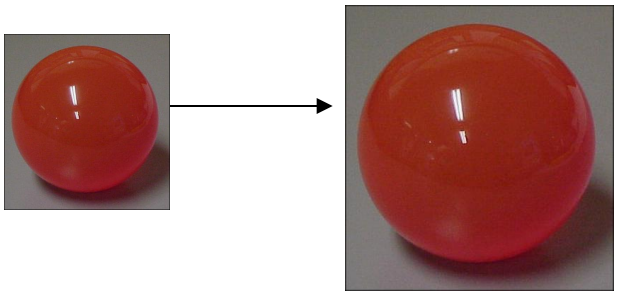
metabolic rate=heat loss rate $\propto$ surface area $\propto$ $(\text{volume})^{2/3}$

↑

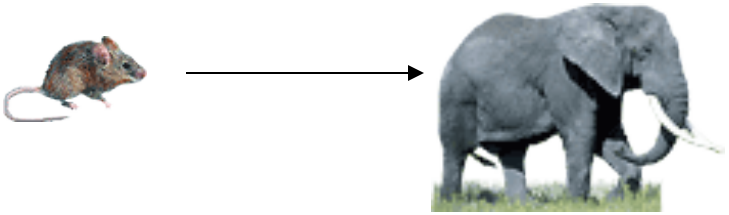
Stefan-Boltzmann law



"isometric scaling"
shape stays same



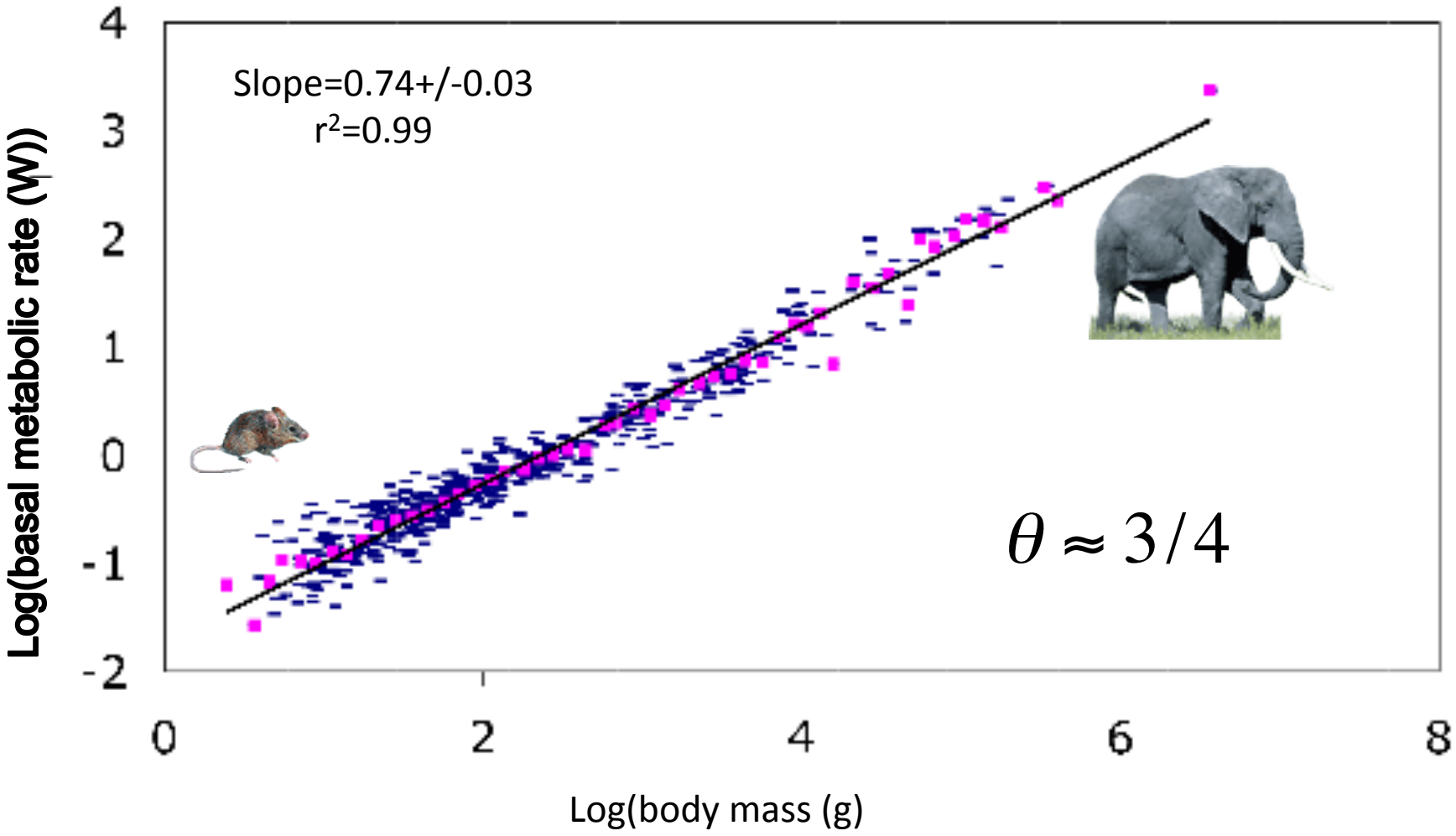
"Allometric scaling"
shape changes



Animals are not isometric, so may not be 2/3

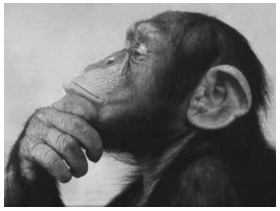
If you were the Matrix, would you choose humans as batteries?

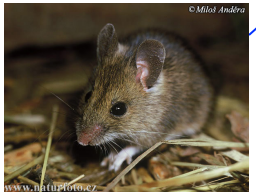
mass dependence of metabolic rate



Savage et al., *Func. Eco.*, 2004

scaling of life stages





	Birth	Reproduction	Senescence	Maximal lifespan
Humans		13.5 yrs	>40 yrs	
Monkeys		4.5 yrs	>20 yrs	
Mice		0.12 yrs	>1 yr	

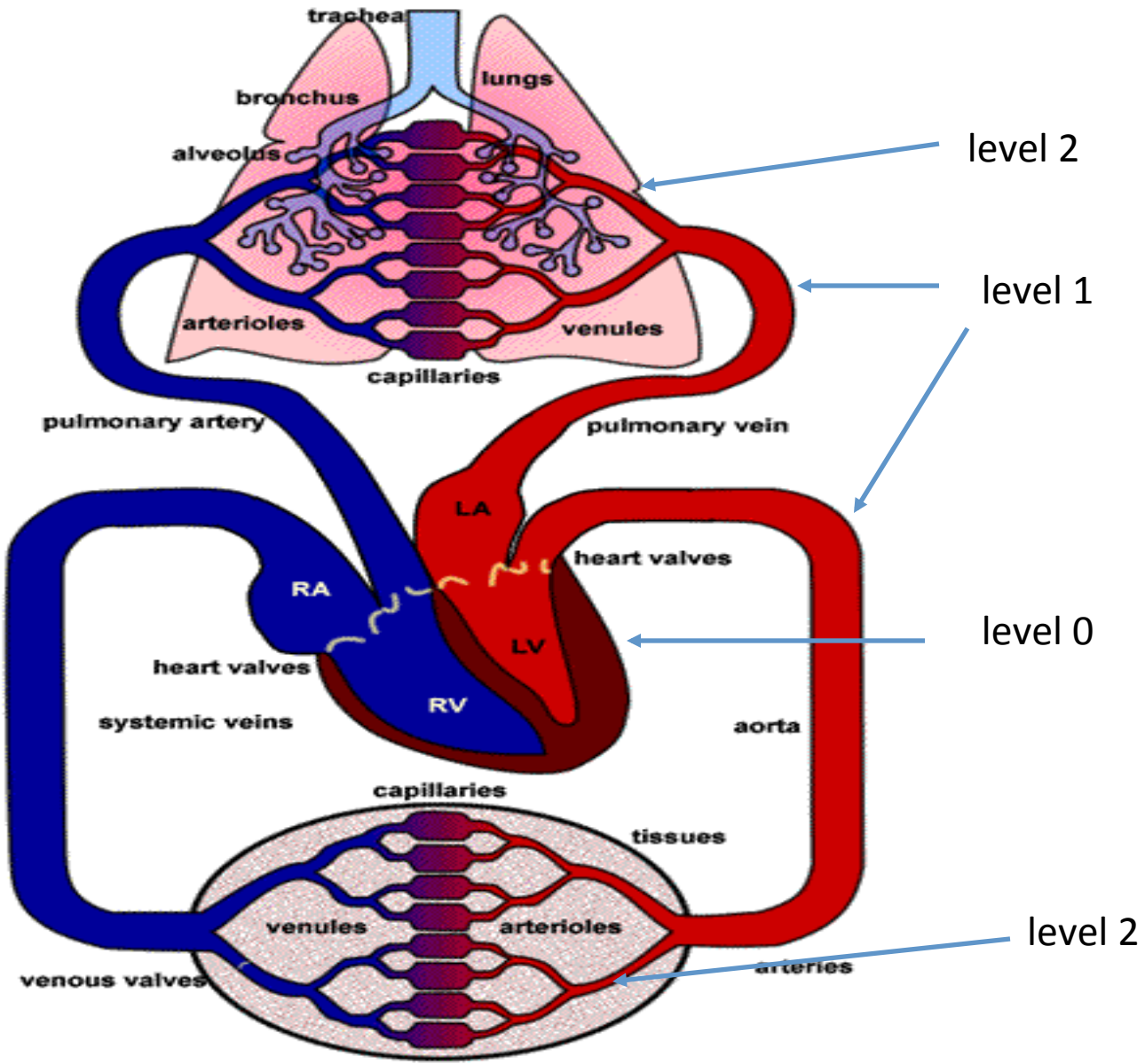
Has been called Kepler's laws for organisms, ecology, etc.

vascular networks

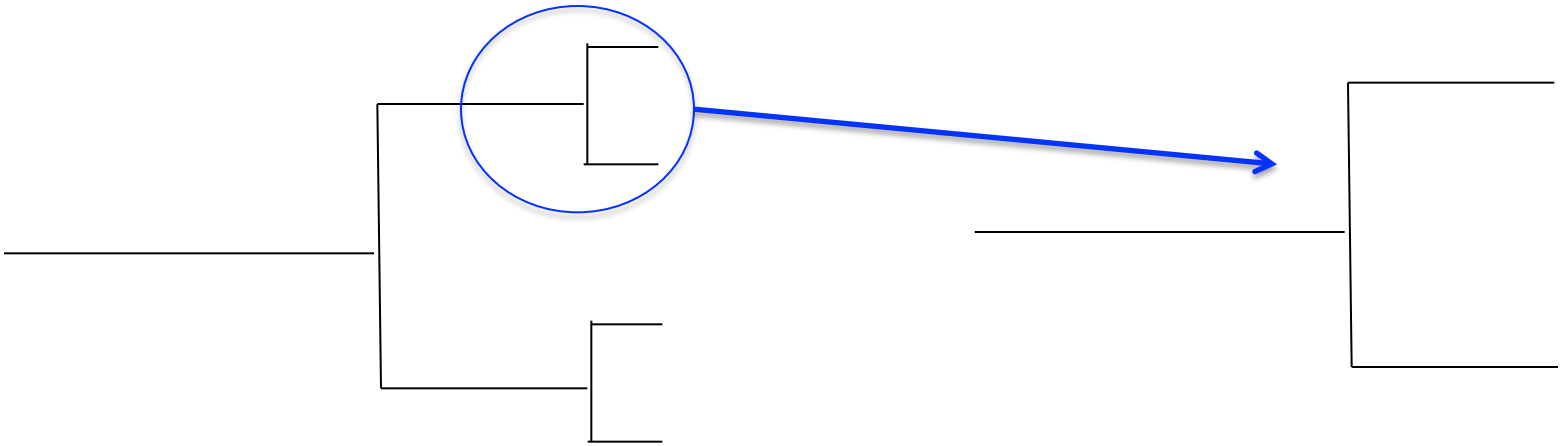
focus on hierarchical, branching network

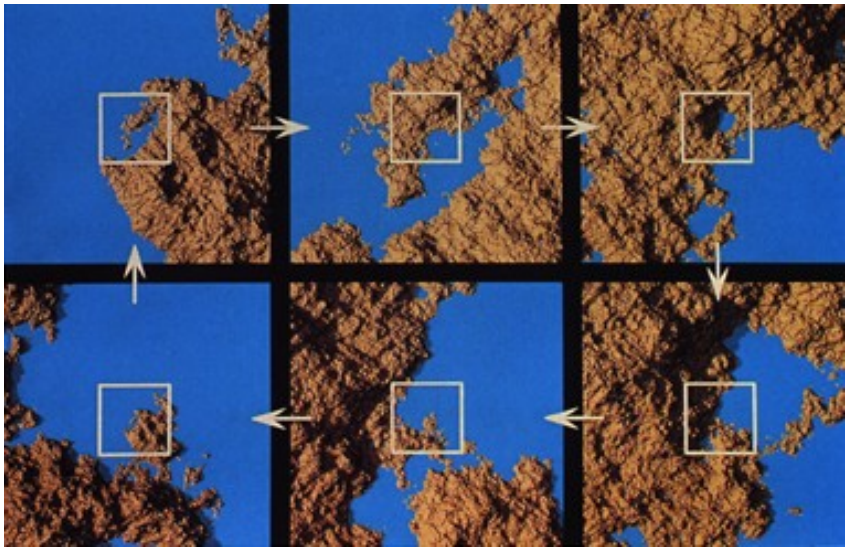
branching ratio

$$n = 2$$



Power laws always tied to self similarity and vice versa (if and only if)





base model has three assumptions

i. Minimization of power to deliver resources

constraint on vessel radii

ii. Space filling to feed all cells

constraint on vessel lengths

iii. Capillaries are invariant in size

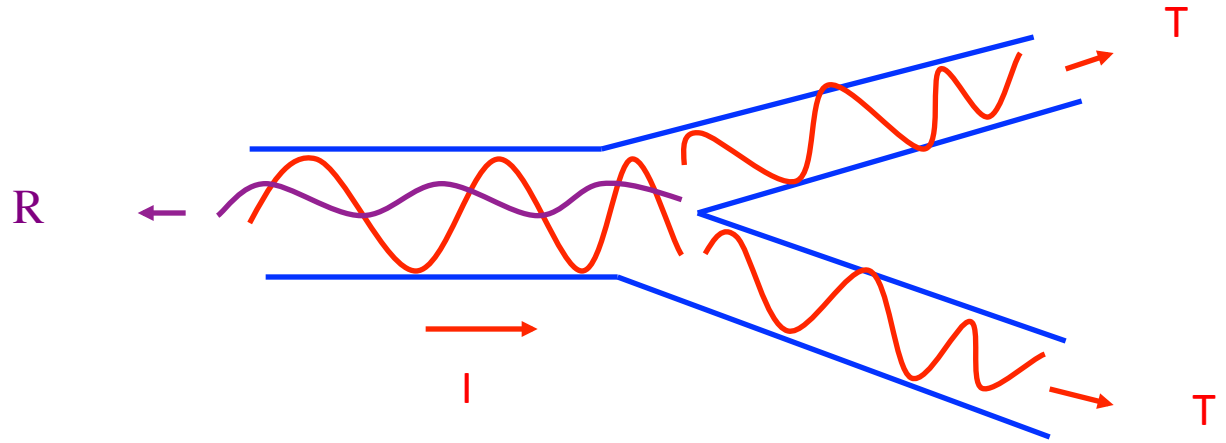
sets overall scale for network

West et al., *Science,* 1997

Savage et al., *PLoS. Comp. Biol.*, 2008

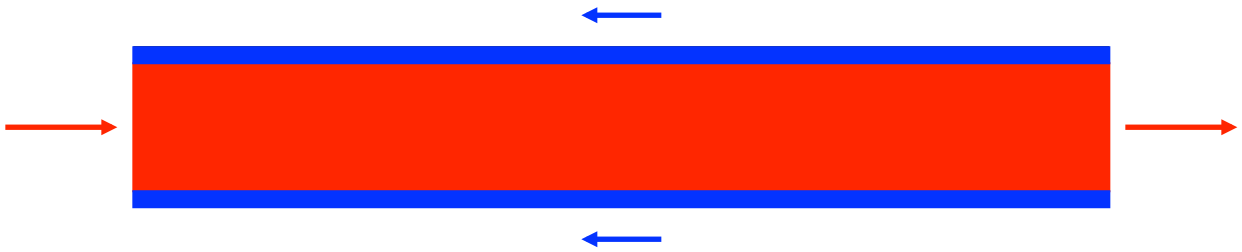
energy minimization

Reflection at junctions (important for larger vessels, pulsatile flow)



$$\beta = \frac{r_{k+1}}{r_k} = n^{-1/2}$$ ← area preserving

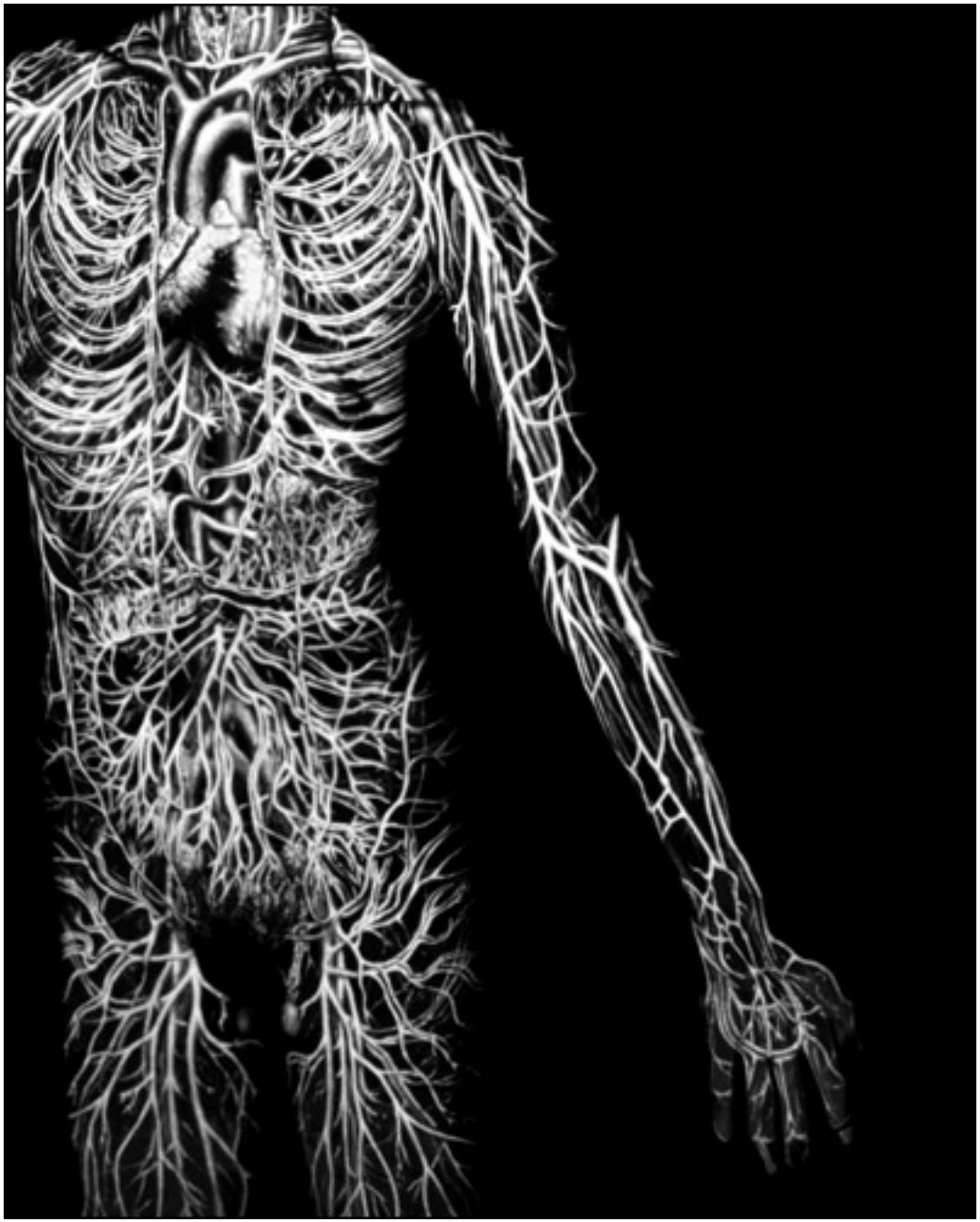
Dissipation (important for small vessels, Poiseuille flow)



$$\beta = \frac{r_{k+1}}{r_k} = n^{-1/3}$$ ← area increasing

West et al., *Science,* 1997

Savage et al., *PLoS. Comp. Biol.*, 2008

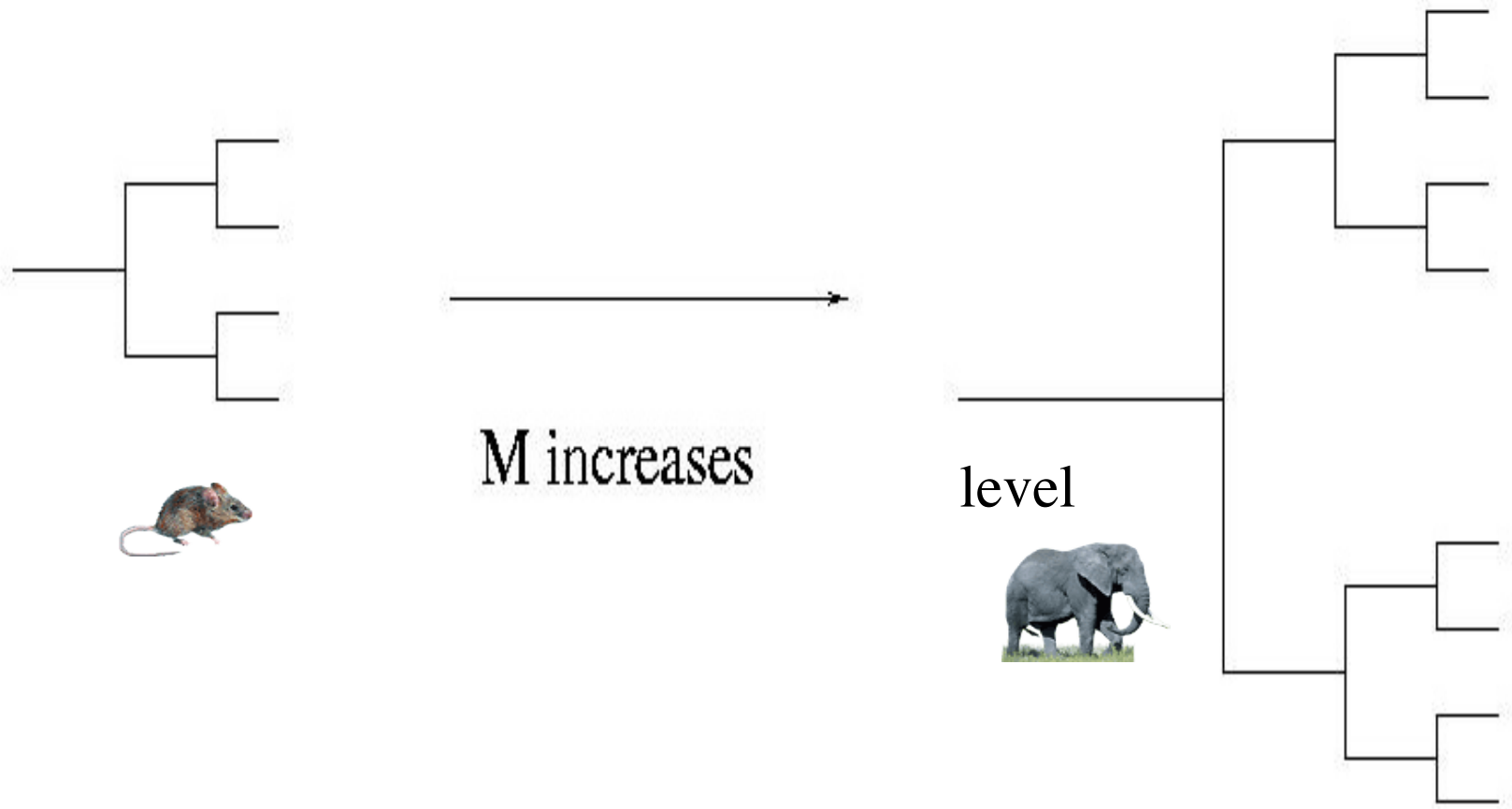


Space-filling,
Hierarchical,
Branching network

$$\gamma = \frac{l_{k+1}}{l_k} = \left(\frac{N_k}{N_{k+1}} \right)^{1/3} = n^{-1/3}$$

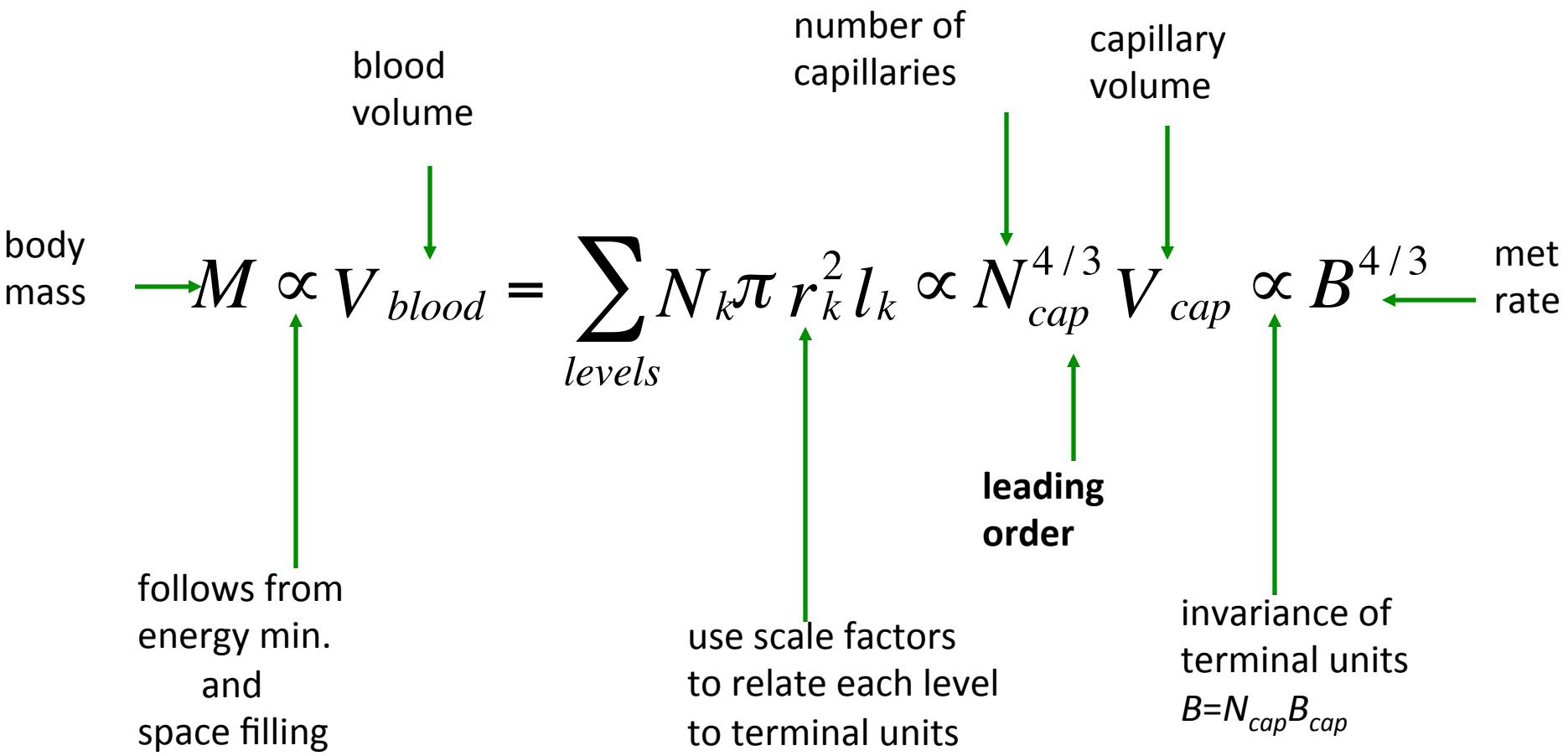
Katherine Du Tiel, 1994

terminal units are invariant



Body size changes network size

metabolic rate and body mass

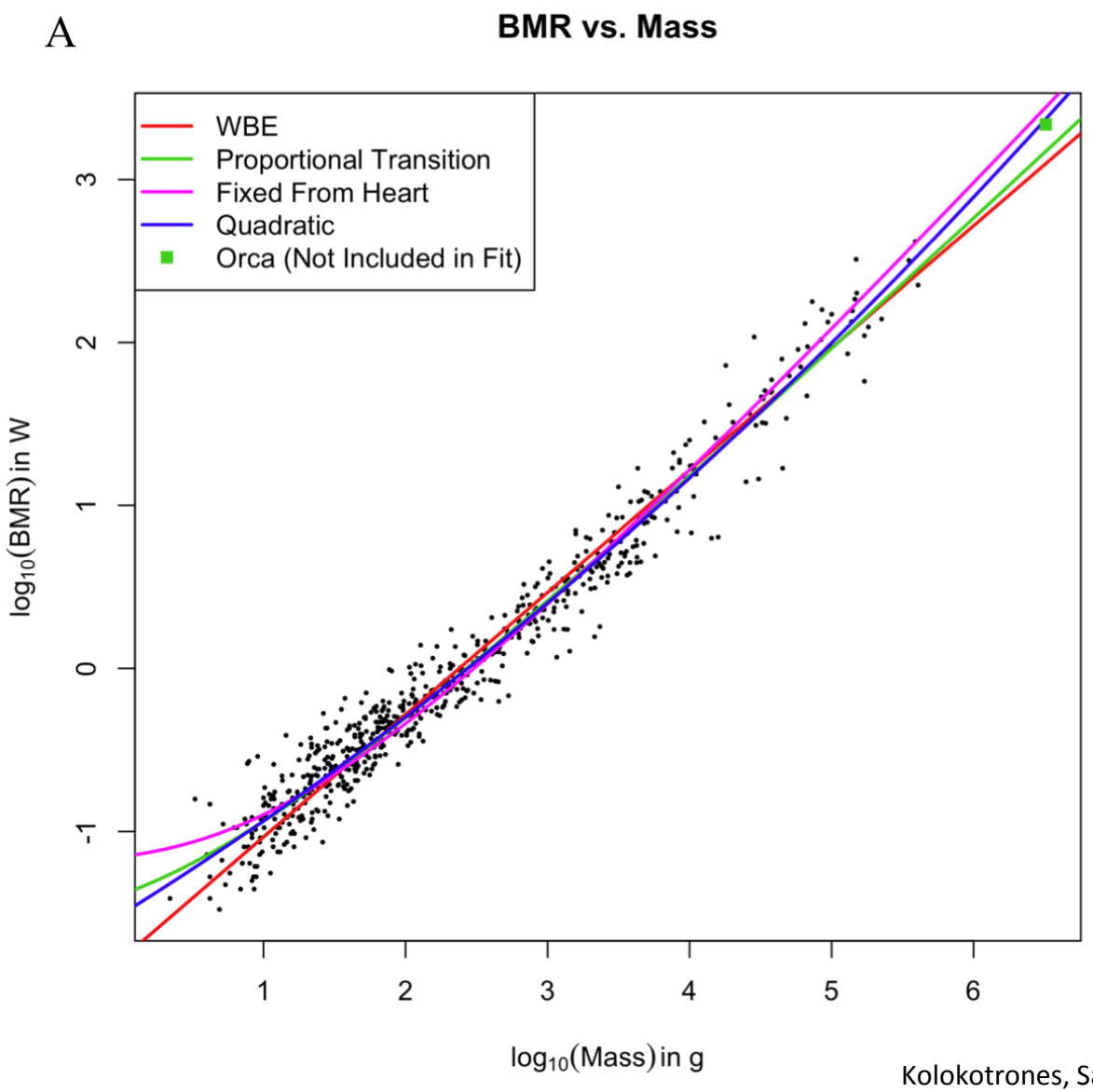


$$B \propto M^{3/4}$$

Replace spherical cow with non-spherical but infinitely large cow.

West et al., *Science,* 1997

deviations from theory

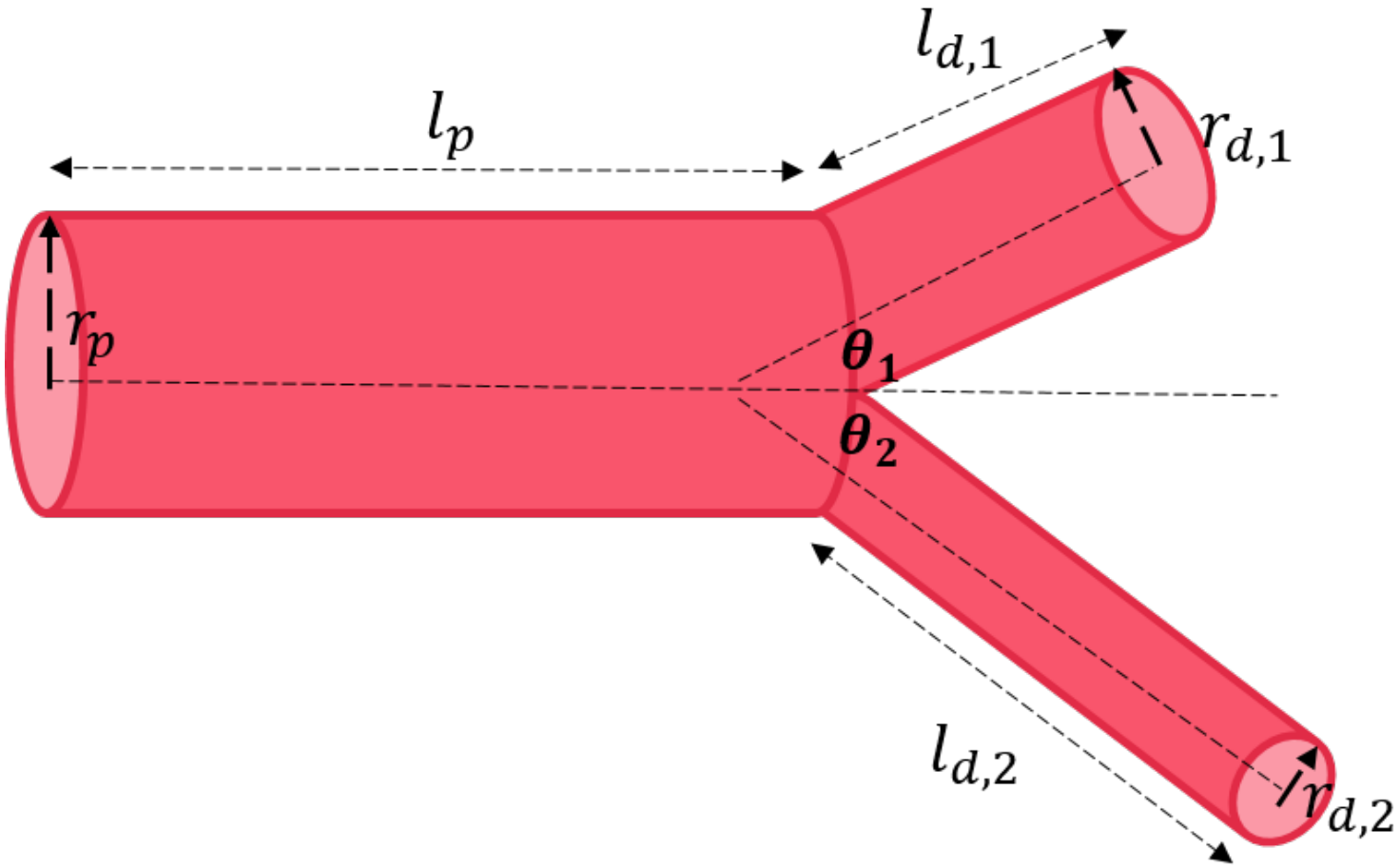


Kolokotrones, Savage, et al., *Nature*, 2012

What is wrong with the vascular models?

Data and tests for self similarity in vascular networks

branching junction measurements



4 measures of scaling exponents—interchangeable?

Conservation Based—LOCAL—single branching junction

$$r_k^a = r_{k+1,S}^a + r_{k+1,B}^a \quad \text{and} \quad l_k^b = l_{k+1,S}^b + l_{k+1,B}^b$$

Ratio Based—LOCAL—single branching junction

$$\beta \equiv \frac{r_{k+1}}{r_k} = n^{-a} \quad \text{and} \quad \gamma \equiv \frac{l_{k+1}}{l_k} = n^{-b}$$

Regression Based—GLOBAL—uses all data across branching levels

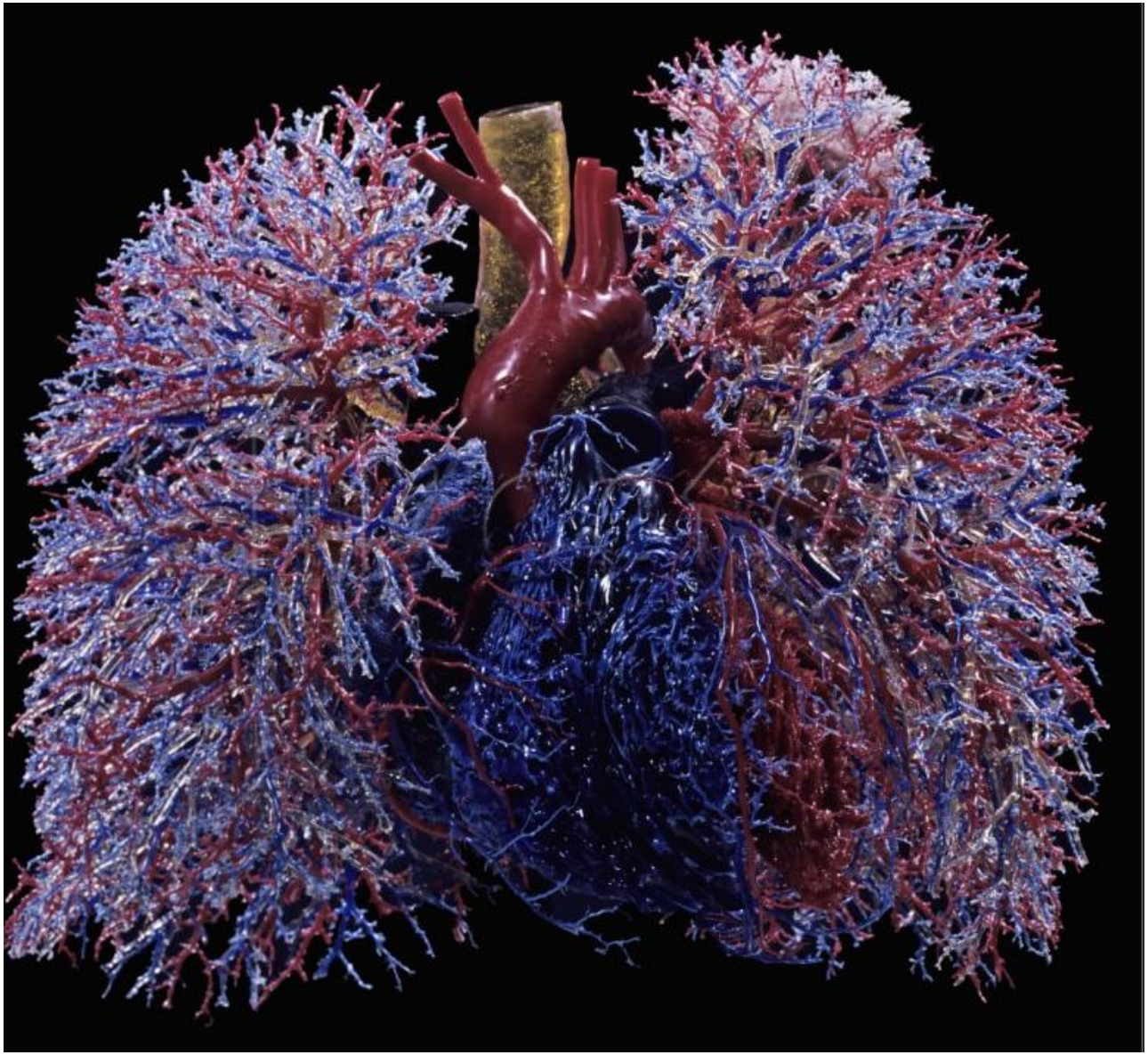
$$r_k \propto N_{tips}^a \quad \text{and} \quad l_k \propto N_{tips}^b$$

Distribution Based—GLOBAL—uses all data across branching levels

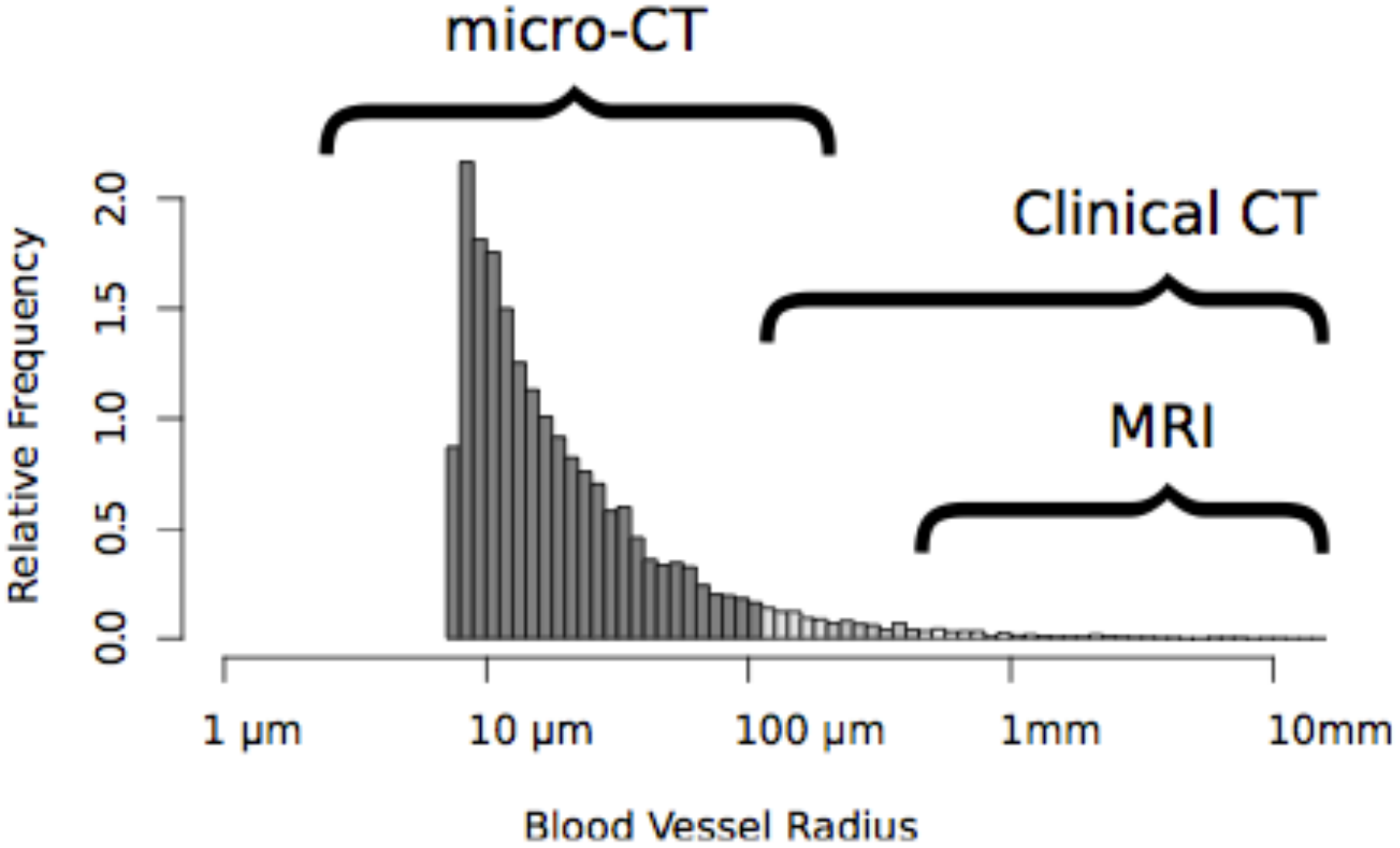
$$P(r_k) \propto r_k^{-1/a} \quad \text{and} \quad P(l_k) \propto l_k^{-1/b}$$

Newberry, Ennis, Savage, *PLoS Comp Biol*, 2015

limited data
destructive casting techniques



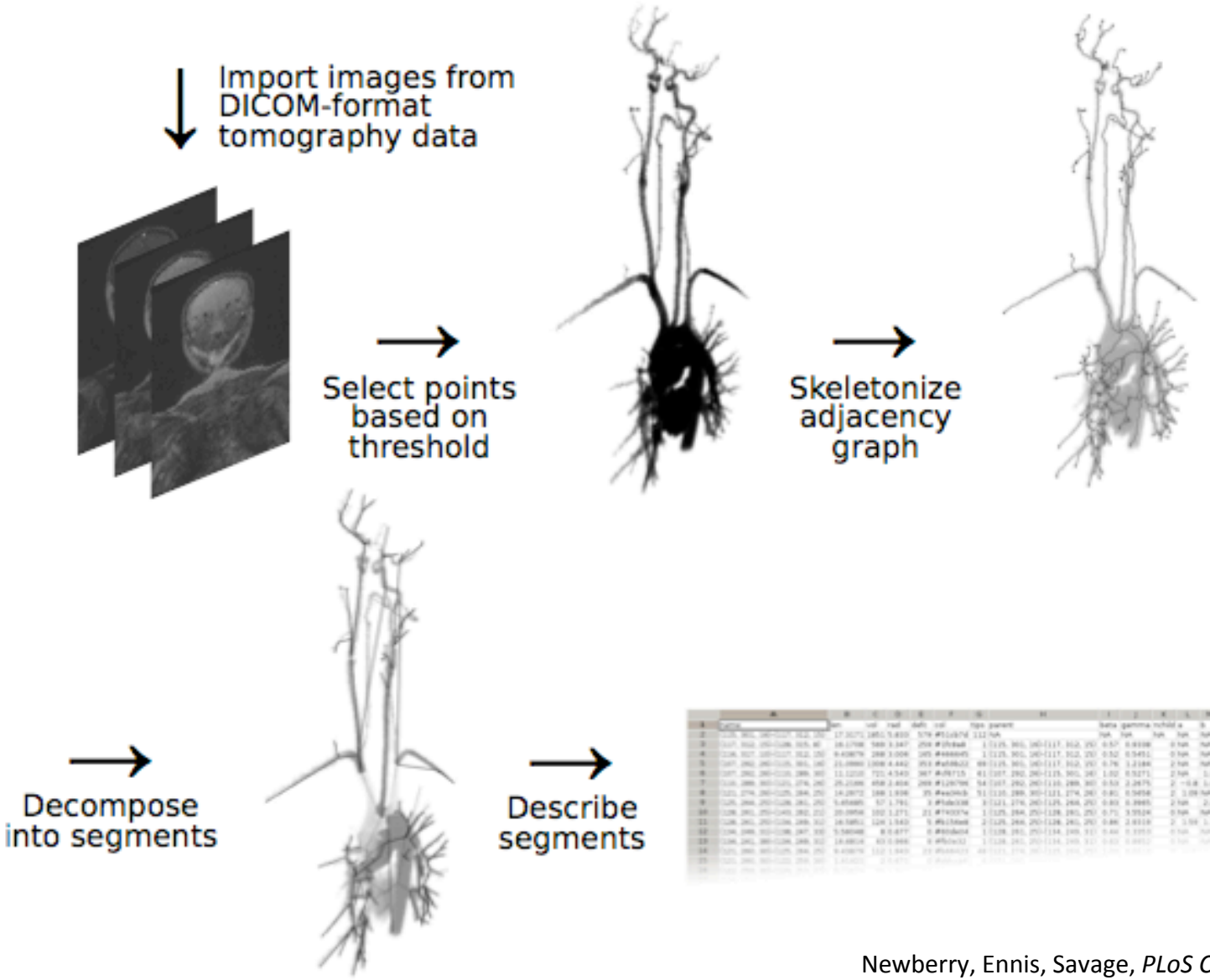
imaging technologies now span full range of vessel sizes



Newberry, Ennis, Savage, *PLoS Comp Biol*, 2015

algorithm for extracting data

steps in algorithm

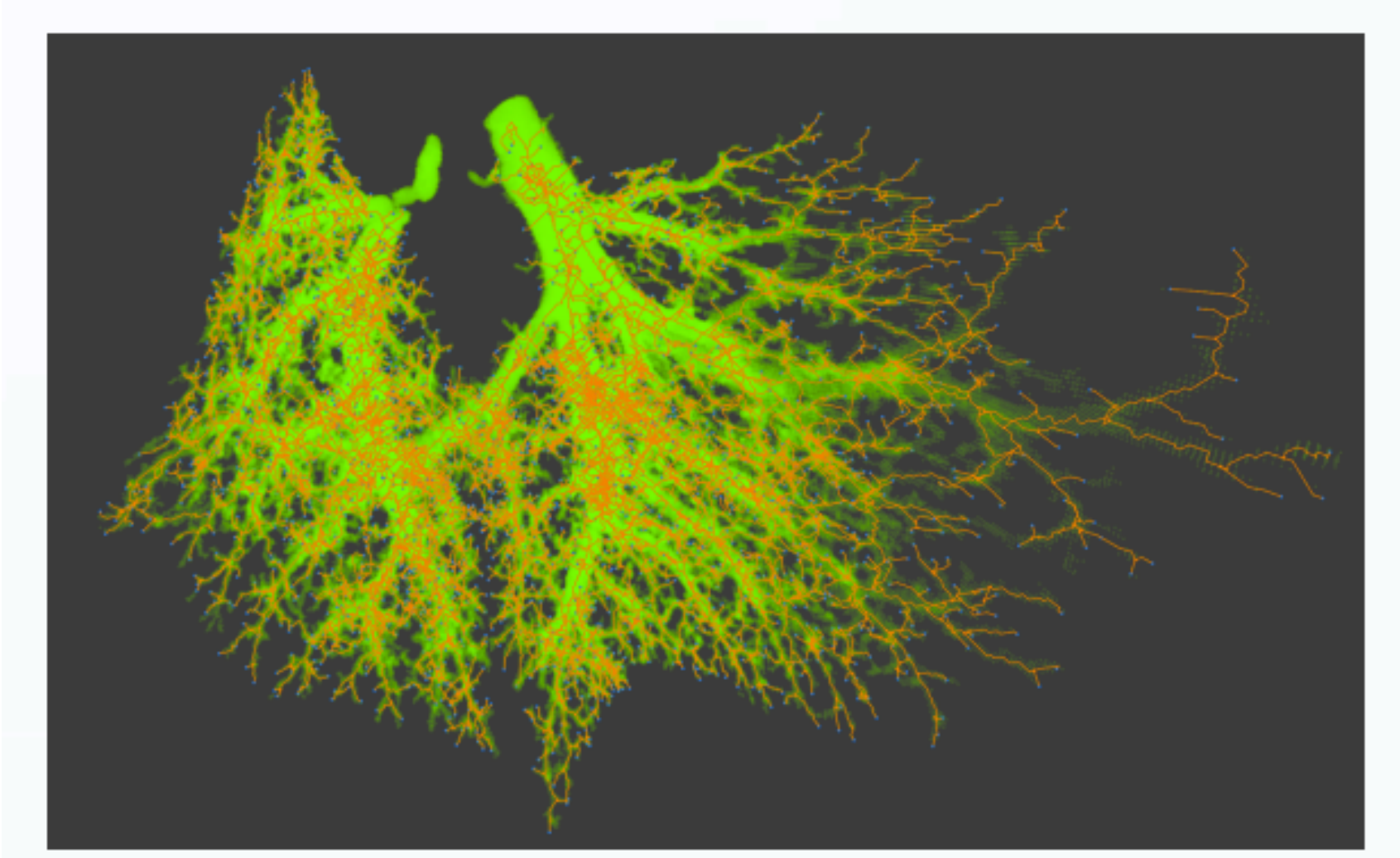


Newberry, Ennis, Savage, *PLoS Comp Biol*, 2015

MRI human head and torso

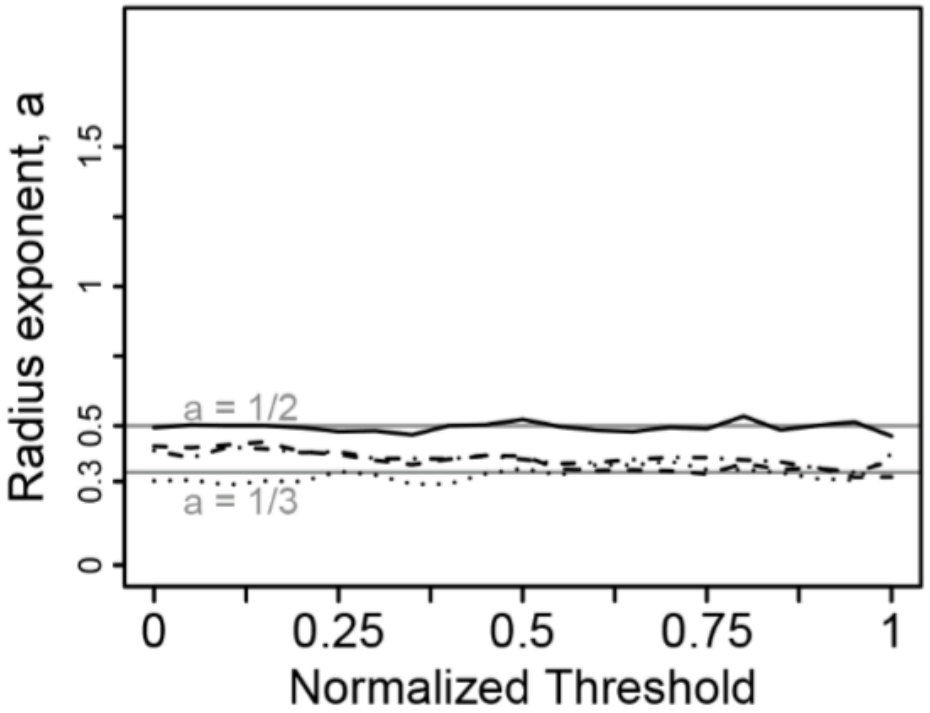
Newberry, Ennis, Savage, *PLoS Comp Biol*, 2015

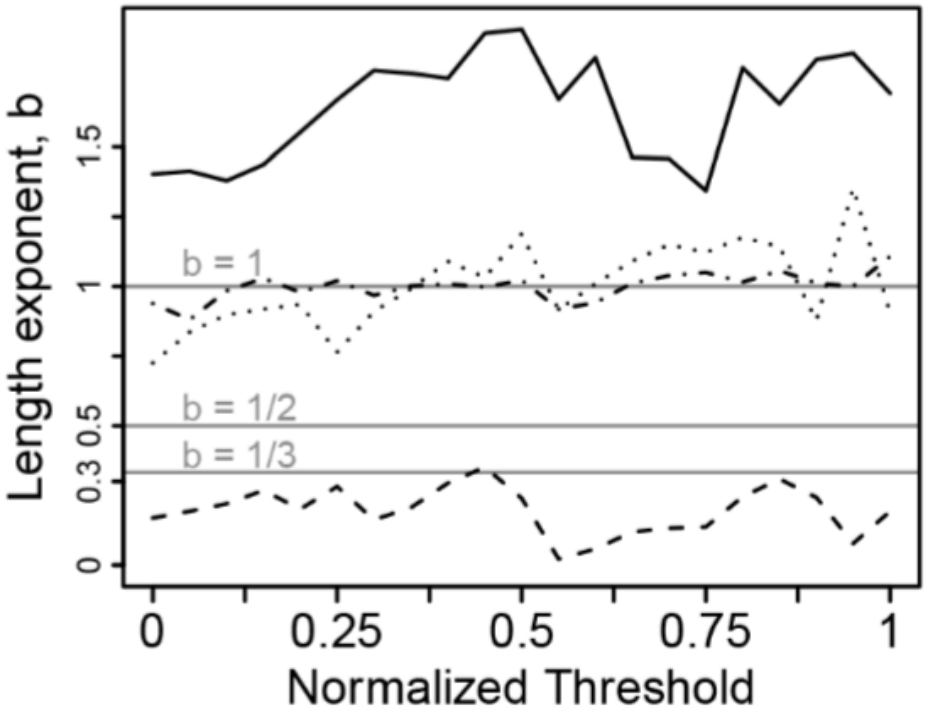
micro-CT mouse lung



Kristina Bostrom's data

results and sensitivity analysis



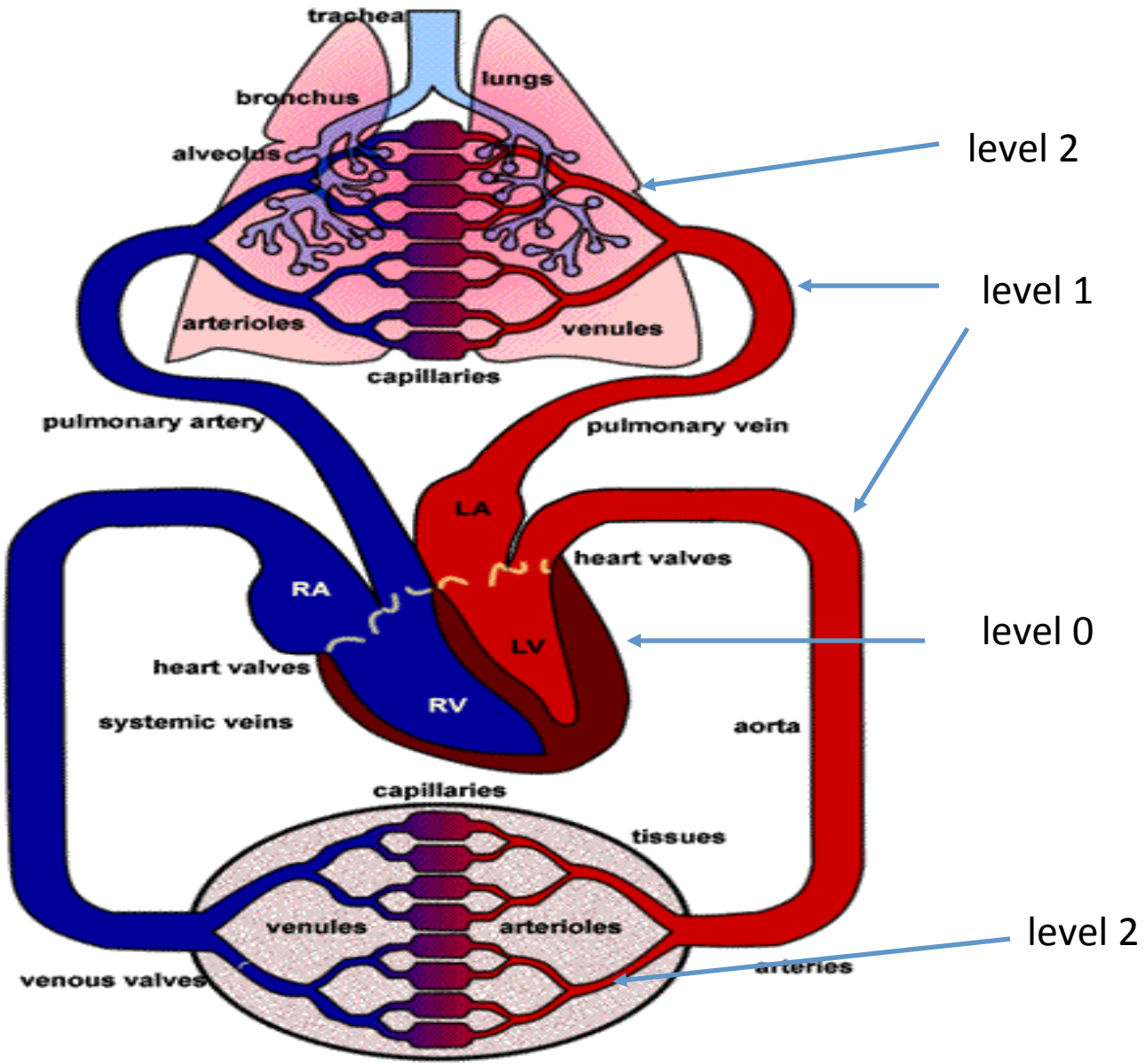


Newberry, Ennis, Savage, *PLoS Comp Biol*, 2015

focus on hierarchical, branching network

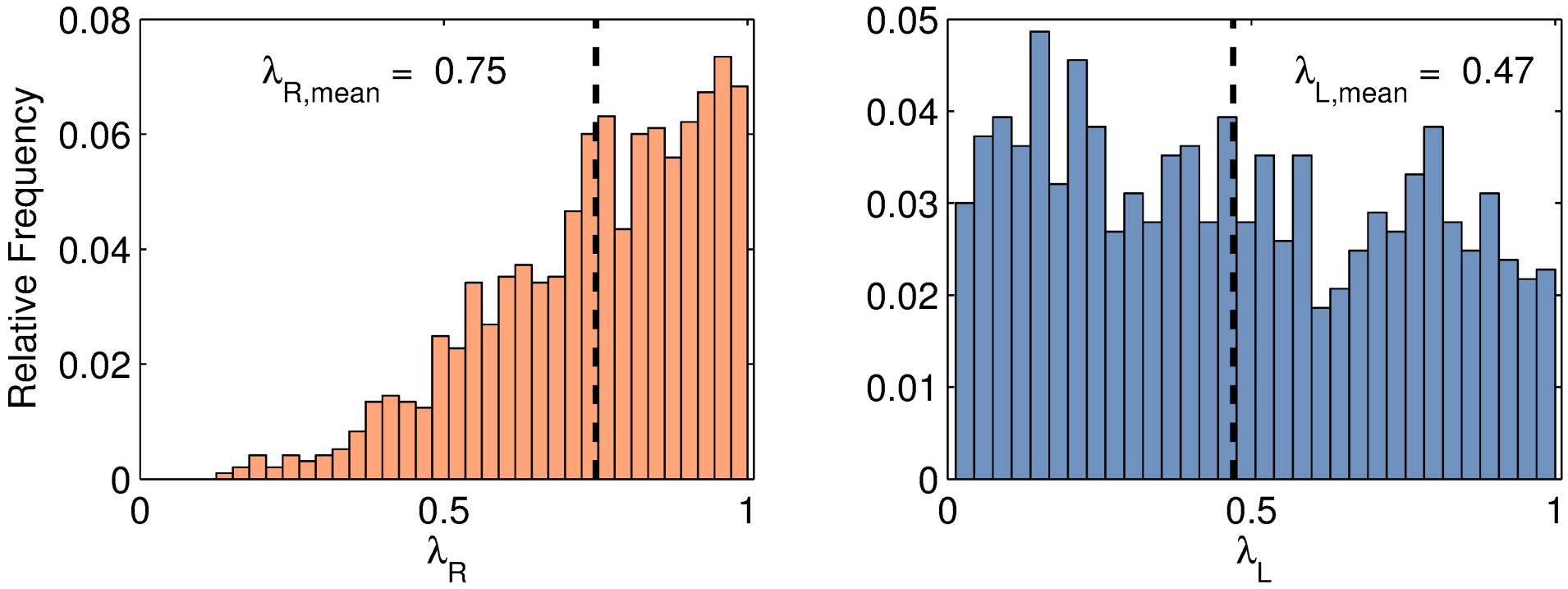
branching ratio

$$n = 2$$



characterizing asymmetry

asymmetry distributions



Ratio of smallest to largest child radius or length at single branching junction
symmetry=1

Hunt and Savage, *Phys. Rev. X*, in review

current and former postdocs

David Hunt

current and former graduate students

Elif Tekin

Mitchell Newberry

current and former undergraduate students

Preeti Chayapathi

Kathryn Burch

Ben Demaree

Angelicia Thomas

Maya Josyula

Shanice Seawright

Quentin Lepak

Matthew Aquilina

Edward Hu

Aditya Athota

Daniel Ennis (Dept. of Radiological Sciences, David Geffen School of Medicine at UCLA)
Kristina Bostrom (Dept. of Medicine, David Geffen School of Medicine at UCLA)