PART 4 Power Laws
Size and the ramp of ascending complexity

Size & complexity: larger size requires greater genetic and anatomical complexity
Large size: more mito, more power, greater metabolic efficiency

Complexity was programmed: evolution to greater complexity by God

<u>If not programmed,</u>
Complexity by chance?
- simply because there was nowhere to go
- pioneering theory: evolutionary success was more likely to be found
  - in the exploitation of new niches

Complexity was inevitable outcome of the workings of natural selection?
- complexity was possible by an immediate payback for an immediate advantage
- but nature seems to favor simplicity (ex. Bacteria)

1. Evolutionary Drift to complexity

Simply a response to the possibilities offered by the environment

2. Any inherent tendency to complexity?

Sex: suggested by Mark Ridley

Energy rather than sex

- the efficiency of energy metabolism
- greater size favored by a lower living cost (the economy of scale)
- Cope's rule: evolutionary trend towards greater size
  - but evolution also favors to smaller as much as larger

Larger size = greater complexity?

- On being the right size (JBS Haldane)
- 10 fold increase in each dimension means
  - surface area: 100-fold increase
  - mass: 1000-fold increase
- if retaining the same metabolic rate
  - 1000 times more oxygen, food, and waste
  - it means 10 times more absorption of food and oxygen through skin
    and 10 times more excretion of waste through kidney

The higher animals are larger than the lower

not because they are more complicated

(they are more complicated because they are larger)

There surely is a limit on being larger in size

Beyond which, only by way of specific adaptations

specialized organs

differentiated cells

There is also advantages on being larger in size

Focusing on cells

larger cells than larger animals

immediate cost: a need for new genes, better organization, more energy

any immediate payback? Power laws of biological scaling

4.1. The power laws of biology

Metabolic rate and Mass

Rat compared to human

- 7 times as much oxygen and nutrients per min
- rat cells must work 7 times harder
- rat must eat 7 times as much food relative to its size

The larger the animal gets, the less it needs to eat per gram weight
Why?

- Max Rubner, 1883
- a log-log plot of metabolic rates of 7 dogs against the weights(3.2~31.2 kgs)
- the slope was mass$^{2/3}$
- explained by the generation of heat and loss (mass & surface area)
- mass & surface area: 1000:100 (3:2 in log-log scale)

Max Kleiber

extended the survey to other species

the slope was ¾ (actually 0.73)

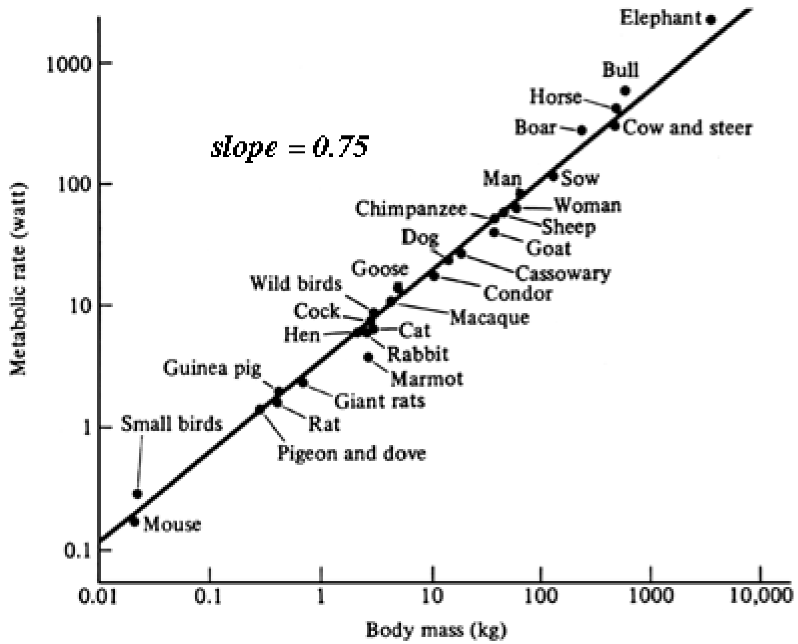
extended even further to plant and single cells

A universal law in biology: quarter-power scaling (Kleiber's law)

Then, why 2/3 or 3/4?

A radical explanation by Geoffrey West, James Brown, Brian Enquist in 1997

based on <u>fractal geometry</u> of branching supply networks (ex. circulatory system)



http://eesc.columbia.edu/courses/ees/life/lectures/lect03.html

http://universe-review.ca/R10-35-metabolic.htm

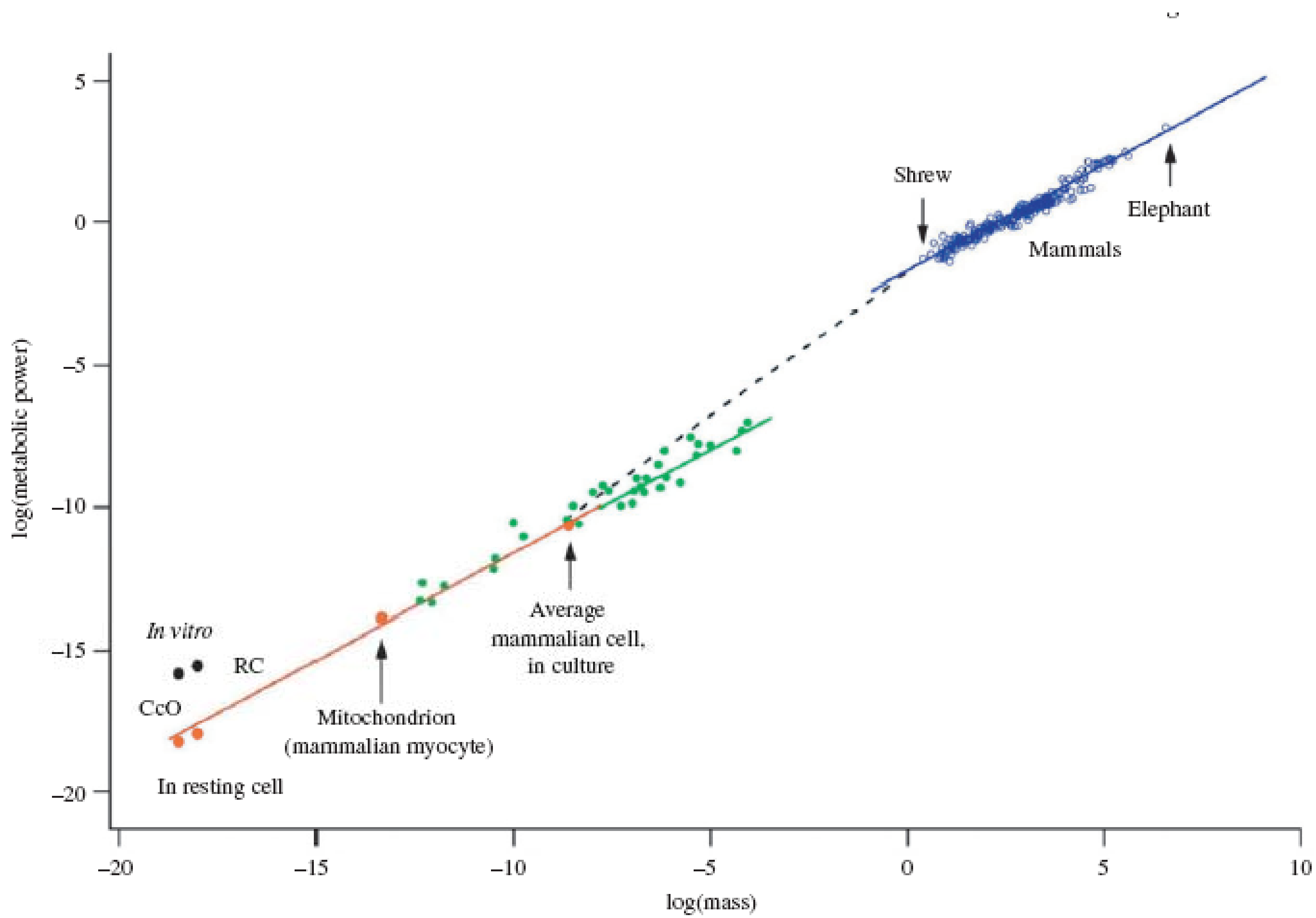


Fig. 2. Extension of Kleiber's 3/4-power law for the metabolic rate of mammals to over 27 orders of magnitude from individuals (blue circles) to uncoupled mammalian cells, mitochondria and terminal oxidase molecules, CcO of the respiratory complex, RC (red circles). Also shown are data for unicellular organisms (green circles). In the region below the smallest mammal (the shrew), scaling is predicted to extrapolate linearly to an isolated cell *in vitro*, as shown by the dotted line. The 3/4-power re-emerges at the cellular and intracellular levels. Figure taken from West et al. (2002b) with permission.

Allometric scaling of metabolic rate from molecules and mitochondria to cells and mammals

PNAS (2002) 99:2473-2478

The fact that metabolic rate scales as the three-quarter power of body mass (*M*) in unicellular, as well as multicellular, organisms suggests that the same principles of biological design operate at multiple levels of organization. We use the framework of a general model of fractal-like distribution networks together with data on energy transformation in mammals to analyze and predict allometric scaling of aerobic metabolism over a remarkable 27 orders of magnitude in mass encompassing four levels of organization: individual organisms, single cells, intact mitochondria, and enzyme molecules. We show that, whereas rates of cellular metabolism *in vivo* scale as $M^{-1/4}$, rates for cells in culture converge to a single predicted value for all mammals regardless of size. Furthermore, a single three-quarter power allometric scaling law characterizes the basal metabolic rates of isolated mammalian cells, mitochondria, and molecules of the respiratory complex; this overlaps with and is indistinguishable from the scaling relationship for unicellular organisms. This observation suggests that aerobic energy transformation at all levels of biological organization is limited by the transport of materials through hierarchical fractal-like networks with the properties specified by the model. We show how the mass of the smallest mammal can be calculated (≈1 g), and the observed numbers and densities of mitochondria and respiratory complexes in mammalian cells can be understood. Extending theoretical and empirical analyses of scaling to suborganismal levels potentially has important implications for cellular structure and function as well as for the metabolic basis of aging.

The fractal tree of life

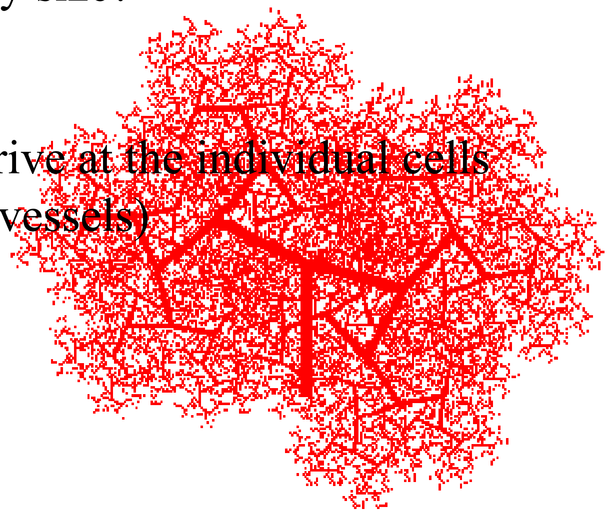
What is fractal geometry? http://en.wikipedia.org/wiki/Fractal

Application to biology

might the fractal geometry of nature's supply networks account for the
universal scaling of metabolic rate with body size?

looks high plausible

because the consumption of food and oxygen arrive at the individual cells
by way of the branching supply network (blood vessels)



According to fractal model

the metabolic rate scale with body mass$^{3/4}$

More radical application to single cells

which seem to lack a supply network
internal architecture: branching networks of cytoskeletons and mitochondria
are they true branching networks?

Universal rules: preferred by physicists who love to use mathematics

are biologists too aware of exceptions?

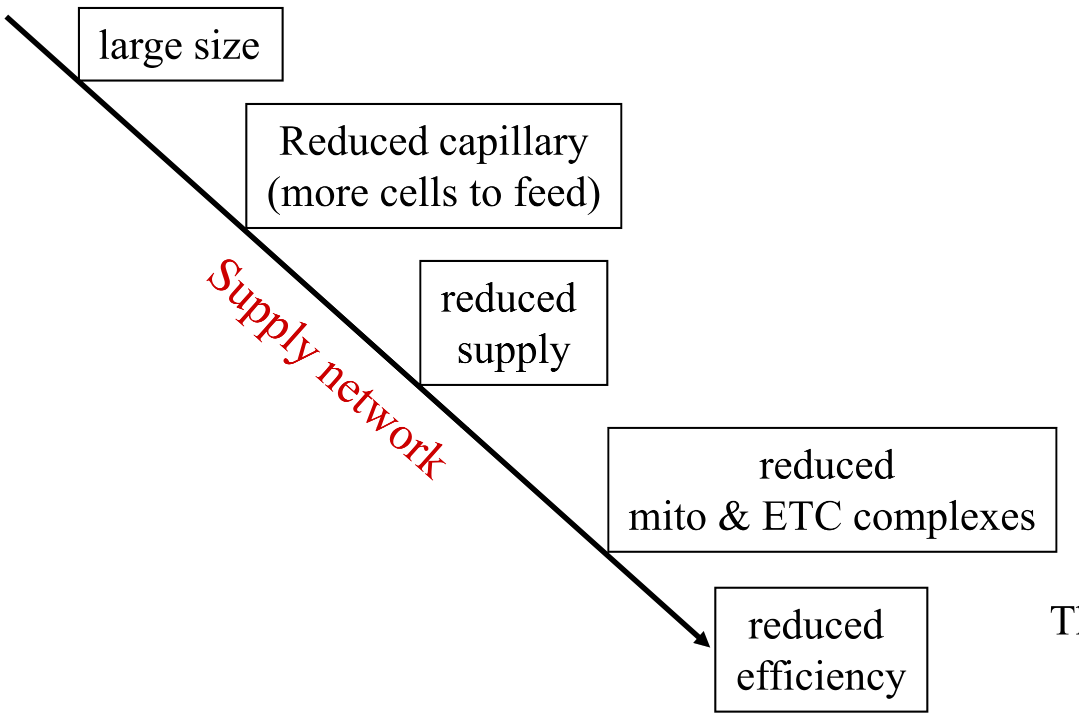
Supply and demand-or demand and supply?

West, Brown, William Woodruff, PNAS (2002)

¼-power rule can be applied to mitochondria and their respiratory complexes

Supply network constrains the metabolic rate,

forcing a particular metabolic rate on individual mitochondria



Then, what use is reduced consuming?

Because supply controls demand?

The reverse may be true:

Compensation not penalty

Questioning the universal constant

*165pp: mammalian cell in culture (meaning the absence of network)

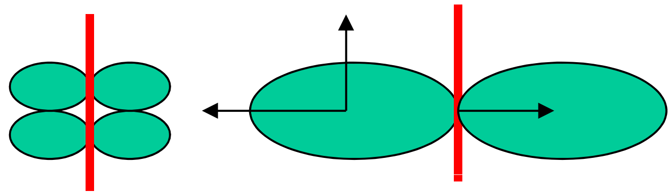
lose mito & depends on fermentation for energy

What if empirical data does not show that the exponent is not 0.75?

Peter Dodds et al. 2001

there are more than 2 slopes depending on individual phyla

The universal constant is a statistical artifact



The limits of network limitation

Supply network (intracellular distribution) limits the upper size of individual cells

A cell colony is supported by separate supply system

Supply network (cardiovascular system) set the upper & lower limits of size

upper limit by oxygen & nutrients

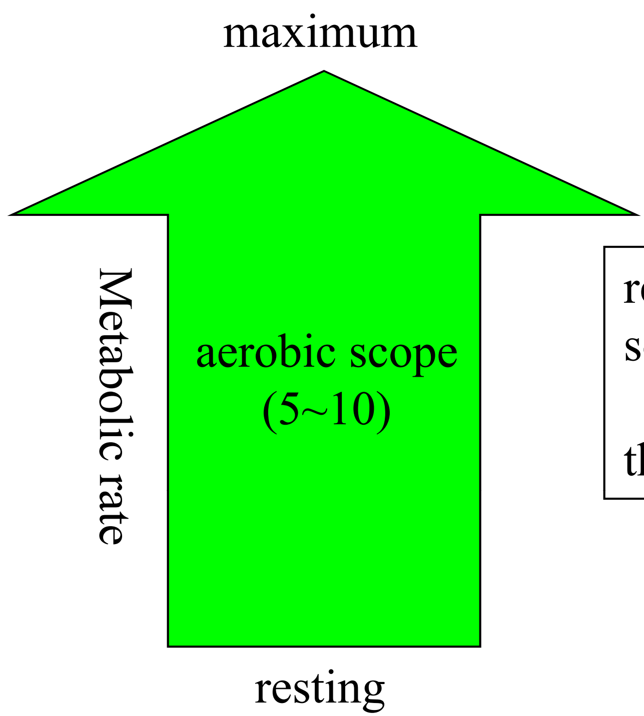
lower limit by solution viscosity versus flow

Within the limits

supply network limits the rate of delivery of oxygen and nutrients?

the answer is NO

Maximum metabolic rate (the limit of aerobic performance)
is limited by the rate of oxygen delivery
but resting metabolic rate is not (what is it?)

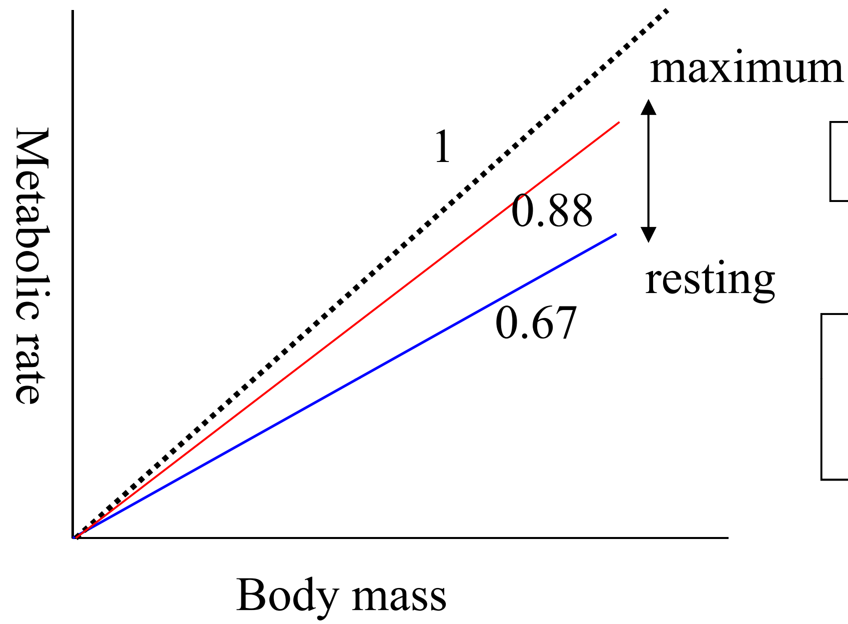


resting and maximum metabolic rates are connected in some way: dependent on each other

then both may scale with size to the power of 0.75

aerobic scope: the increase in oxygen consumption from resting to maximal metabolic rate

The slope of 0.88 for maximal metabolic rate does not coincide with the prediction (0.75) of the fractal model



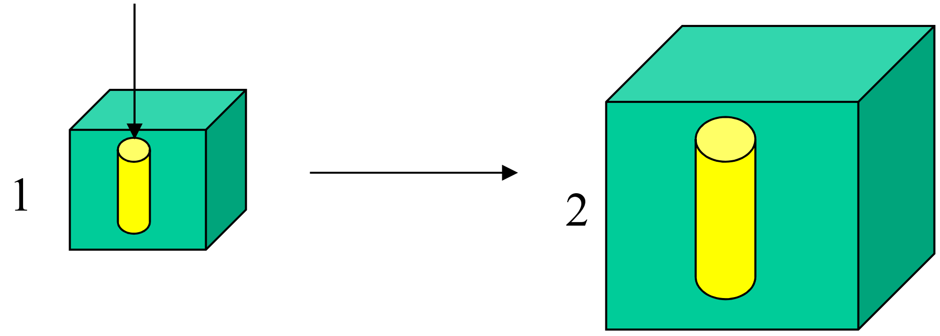
aerobic scope rises with body size

larger animals have greater reserve of stamina & power

Just ask more

Why does the maximal metabolic rate scale with a higher exponent?
The closer to 1, the closer to retaining the same cellular metabolic power

Skeletal muscle strength: proportional to the cross-sectional area



mass: 2^3 muscle strength: 2^2

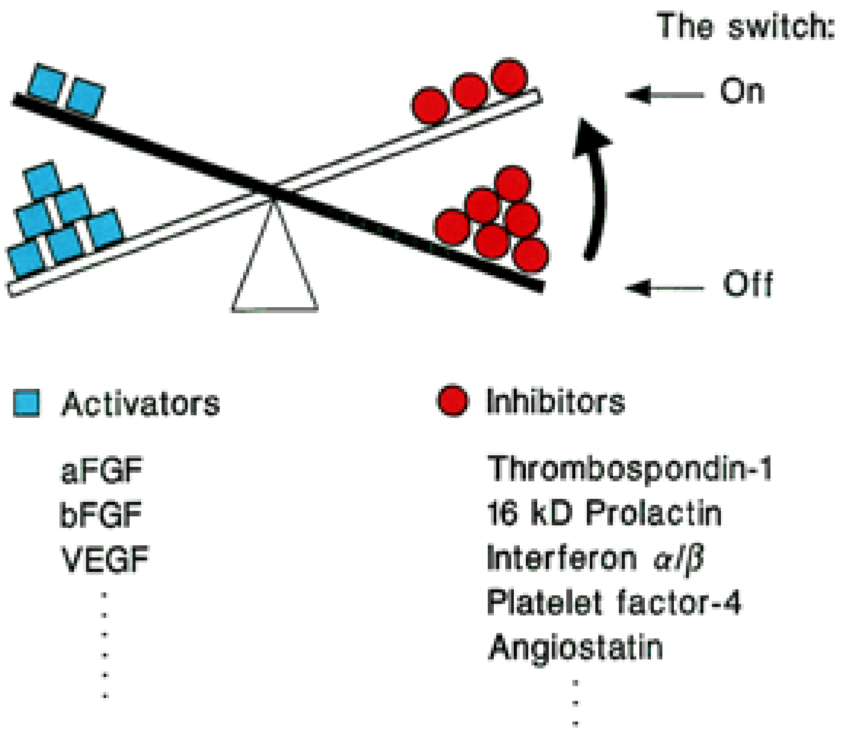
The larger, the weaker relative to the size Is it inevitable?

If fractal geometry applies, capillary density decrease at the scale of 2/3 exponent
It is not true. The capillary network hardly changes as body size rises.
Each capillary serves about the same number of cells in skeletal muscle.

The capillary density depends on the tissue demand,
not on the limitations of a fractal supply network

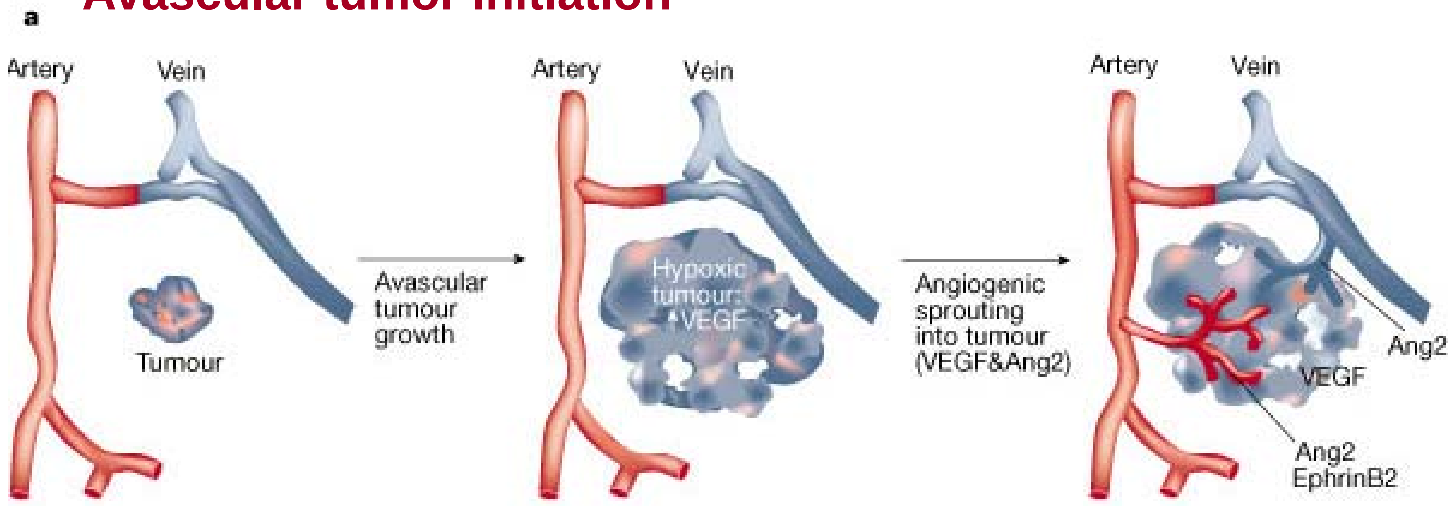
Hypoxia tissue cells signal: angiogenesis
physiological (exercise, high altitude) & pathological (cancer)

THE BALANCE HYPOTHESIS FOR THE ANGIOGENIC SWITCH

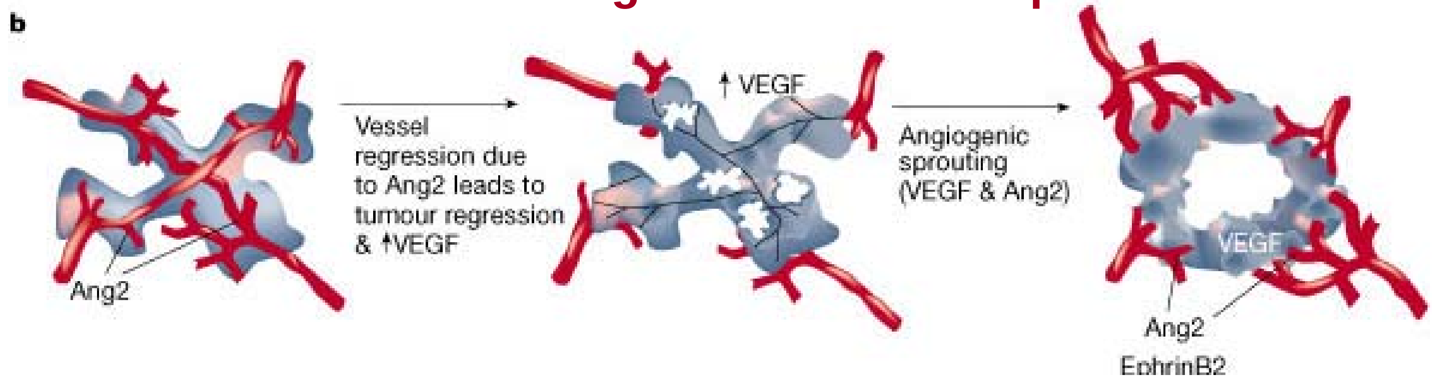


Models of tumour angiogenesis

Avascular tumor initiation



Tumor initiation involving host vessel co-option



High demand, high oxygen concentration

high flow, high RBC, high hemoglobin

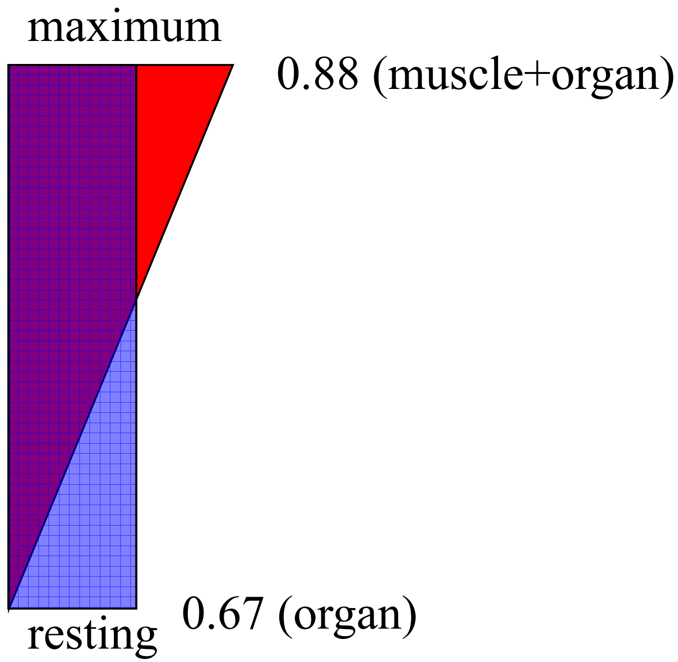
oxygen concentration in blood does not change (maybe toxic)

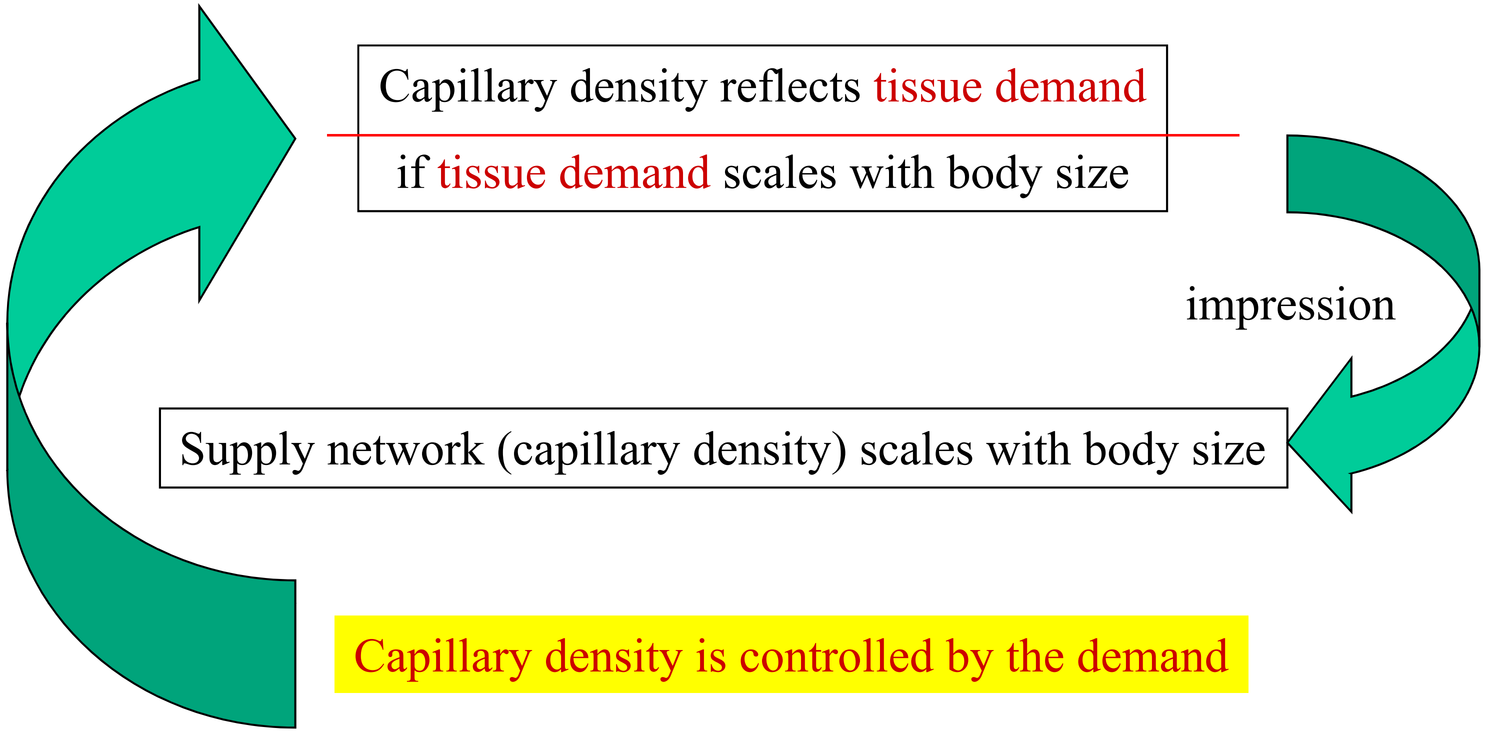
Diversion of blood to and from the skeletal muscle

during resting & maximum metabolic rate

Each muscle cell has the same power, regardless of the size of the animal

scale with mass to the power of 1 (why 0.88?)




Capillary density reflects tissue demand
if tissue demand scales with body size
impression
Supply network (capillary density) scales with body size
Capillary density is controlled by the demand

Part and parcel of metabolism

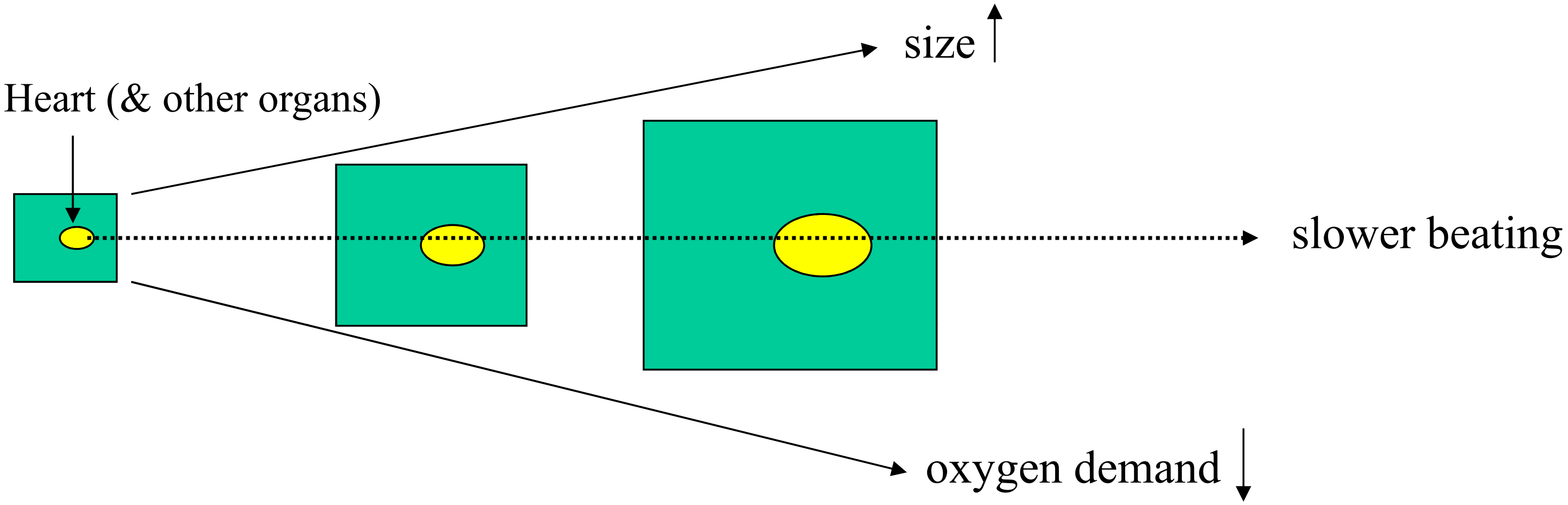
The meaning of low resting metabolic rate

energy demand of cells falls with size (energetic efficiency),

which applies to all eukaryotes

Why?

Any evidence to show that greater size actually yields efficiencies rather than constraints?



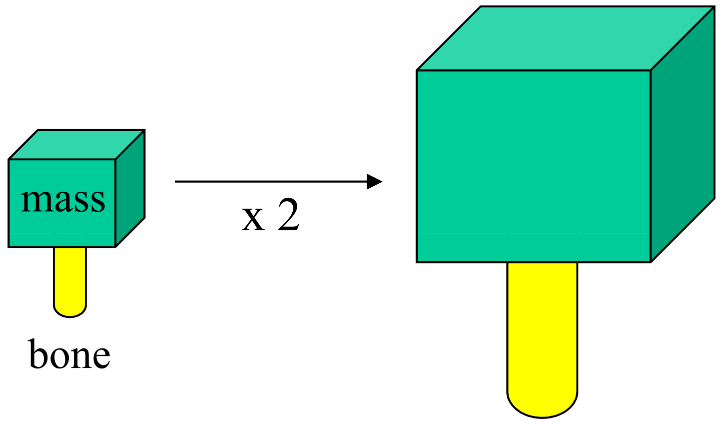
Heart contributes to resting metabolic rate

constant heart size relative to the body mass

but slower beating, because oxygen demand to other tissues has fallen

becomes faster, if demand increases

Bone: different response to increase in body size
metabolically inert
strength depends on the cross-sectional area



$$\frac{\text{mass: 2x2x2}}{\text{cross-sectional area: 2x2}} = 2 \text{ (required bone strength)}$$

$$\frac{\text{mass: 2x2x2}}{\text{cross-sectional area: 2x2x2}} = 1 \text{ (bone strength)}$$

If bone quality is identical,
bone mass (quantitative): 2^3 (cross-sectional area) x 2 (length) = 2^4

Bone takes up a greater proportion of body mass
The scaling exponent: 4/3
The real value is 1.08 (bone quality)

→ limit size in terrestrial animals

body:	2x2x2=8	4x4x4 = 64	8x8x8=512
bone:	1x1x1x1=1	2x2x2x2 = 16	4x4x4x4=256
ratio:	0.125	0.25	0.5

body is filled with more inert material
Scaling of metabolic rate with size = exponent of 0.92
is it enough?
liver or kidney function may have a threshold
 the relative size falls as body rises
 (ex. Mouse liver, 5.5%; rat, 4%; pony, 0.5%)
 metabolic rate varies
 (ex. Mouse liver cells are 9 times higher than horse cells)

the resting metabolic rate of an animal is composed of many components
yet the trial of mathematical calculation is incomplete

Metabolic demand falls with size, and the demand controls supply network, not the other way around

4.2. The warm-blooded revolution

Chemically, temp increases metabolic rate

Endothermy: dependent on the activity of their organs

  muscle contribution in mammals

Ectothermy: gain body heat from the surroundings

Endothermic animals needs 6~10 times as much fuel to maintain temperature

There are serious and immediate costs to raising body temp

How do we explain the rise of endothermy in mammals and birds?

<u>Aerobic capacity hypothesis: Albert Bennett & John Ruben, Science (1979)</u>

Two assumptions:

1. Initial advantage was related to speed & endurance (power)
   - due to maximum metabolic rate & muscle performance
   - not resting metabolic rate & temp
2. There is connection between maximum & resting metabolic rate (recovery)

Suggestion:

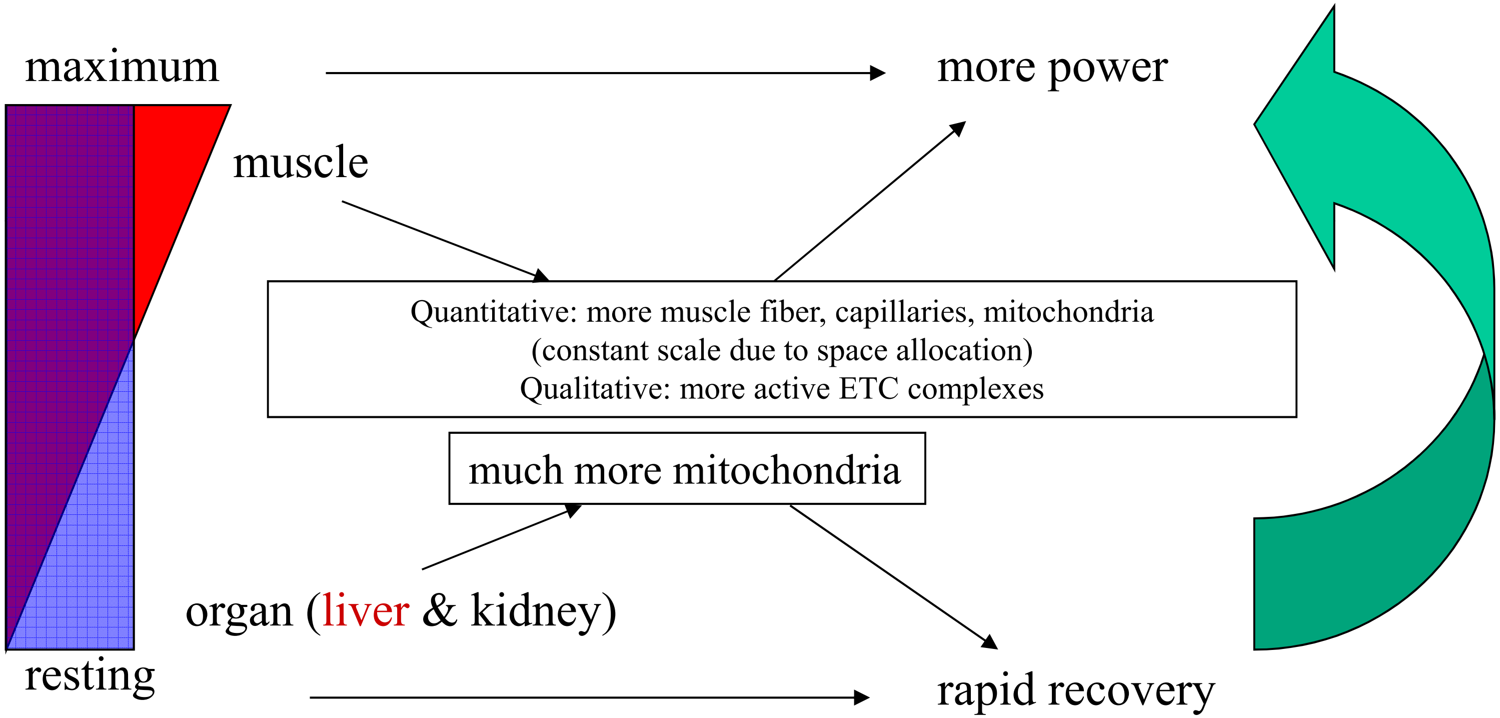
- resting metabolic rate was elevated to the point that
  - internal heat production could raise body temperature
- the advantage of endothermy was selected for their own benefit

Sizing up to complexity

The selective advantages of increased activity are not subtle but rather are central to survival and reproduction

To improve speed & stamina
- quantitative & qualitative changes in the aerobic power of skeletal muscle
- more muscle fibers, capillaries, mitochondria, ETC complexes
- greater mitochondrial power & faster maximum metabolic rate

Link between maximum & resting metabolic rate?
- mammalian organs contain 5 times as many mito as an equivalent lizard
- speedy recovery from aerobic exertion

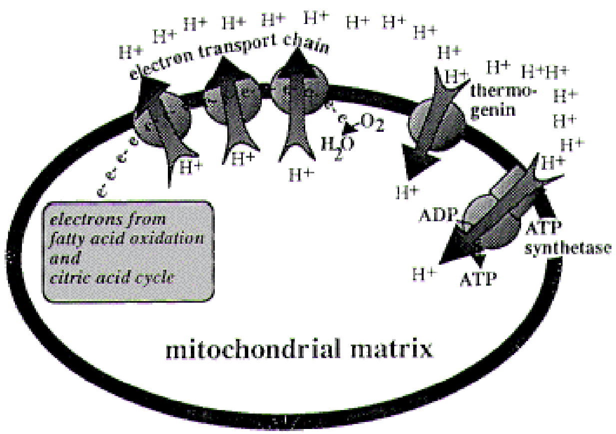


Proton leak

During rest diversion of blood flow from skeletal muscle to organs
Especially after a meal, blood is rich in nutrients

Martin Brand & John Speakman
uncoupled & surviving

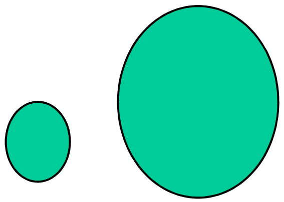
Heat production might have been a byproduct
But evolved to endothermy in large mammals,
which can balance heat production with heat loss
Small animals need supplementary adjustment: brown fat
resting metabolic activity not for muscular capacity
but for heat loss



Large animals:
metabolic power to balance muscular demand

Small animals:
metabolic power to maintain body temp

high surface area: high heat loss



First steps up the lamp

The larger, the higher energetic efficiency: the immediate reward of energetic efficiency

1. at the level of individuals not on a cell-by-cell or gram-weight basis
   rat eat more than us but less powerful than us

2. How about single cells?
   intracellular modular system
   larger nucleus-larger DNA-raw material for complexity
   economics of scale: energetic efficiency & modular system