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?

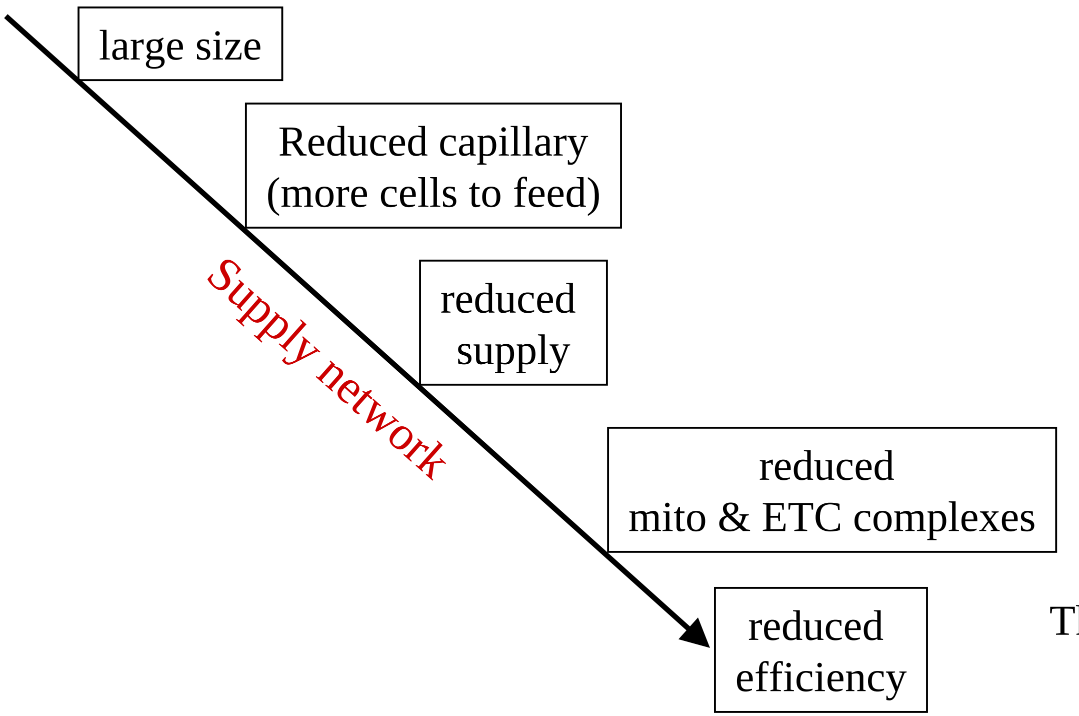
Supply and demand-or demand and supply?

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

Questioning the universal constant

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

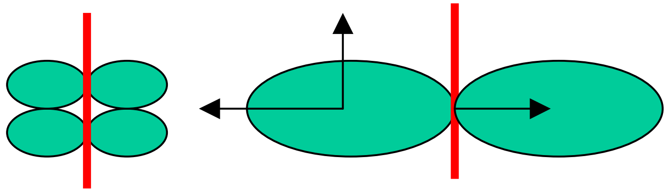
lose mito & depends on fermentation for energy

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 artefact



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

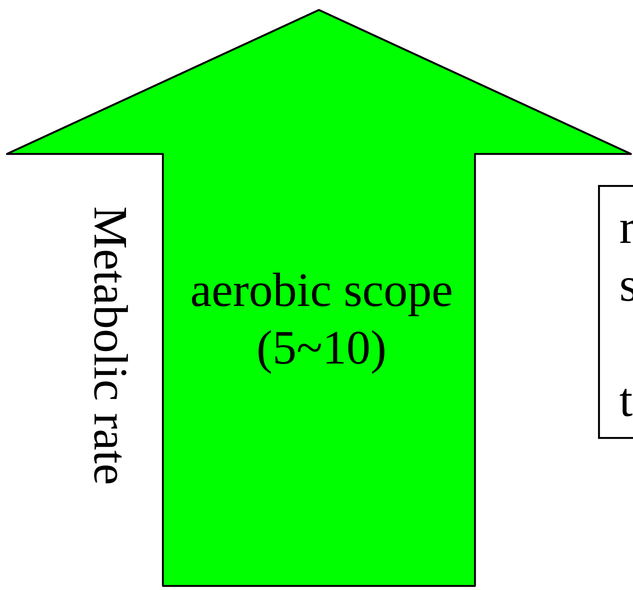
Within the limits

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?)

maximum



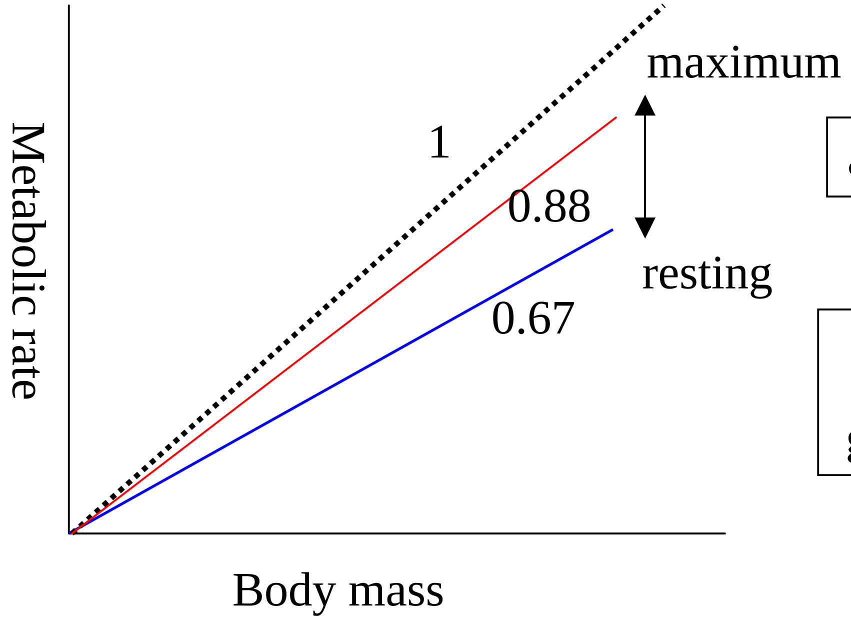
resting

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

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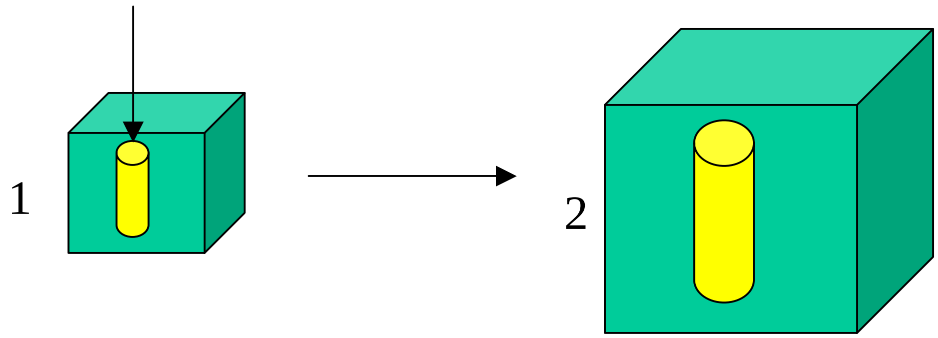
Skeletal muscle strength: proportional to the cross-sectional area



mass: 2^3
muscle strength: 2^2

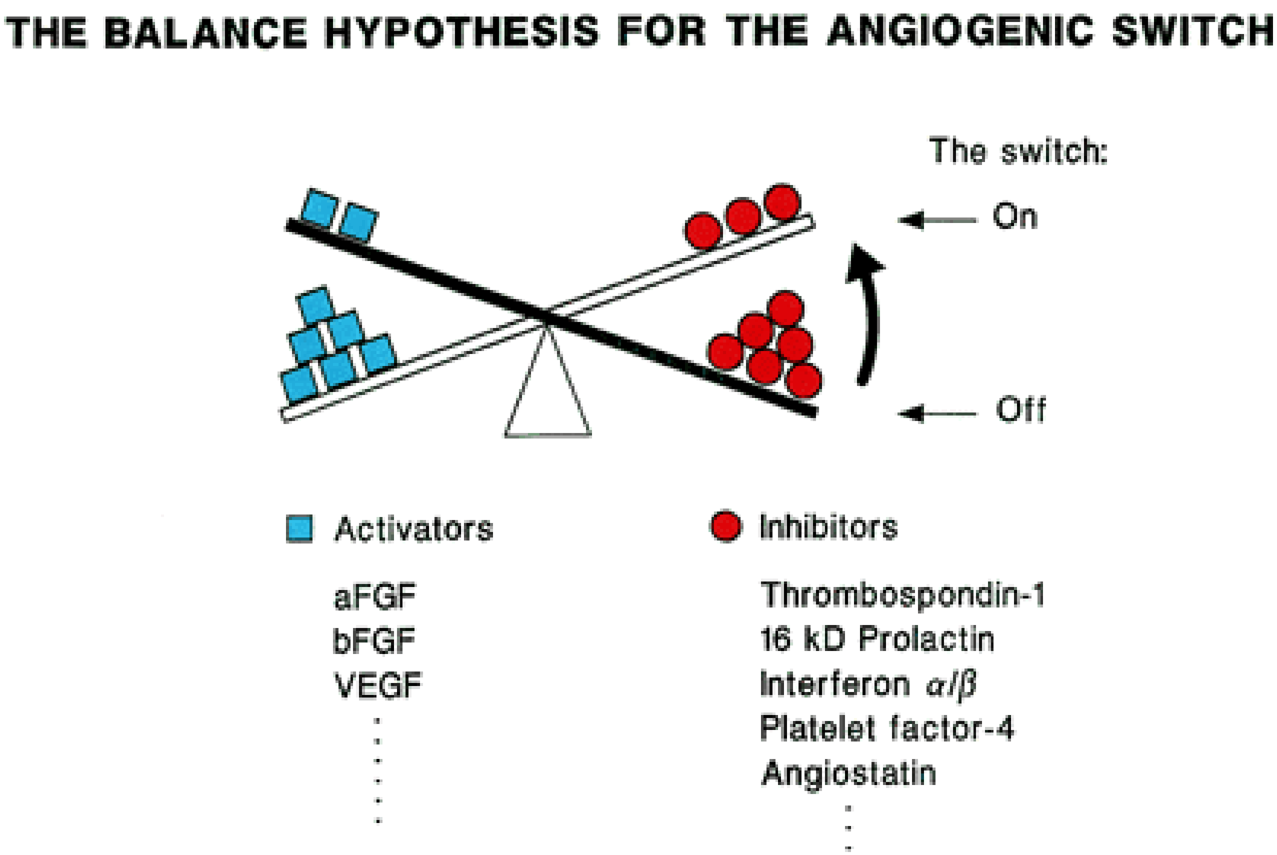
→

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.

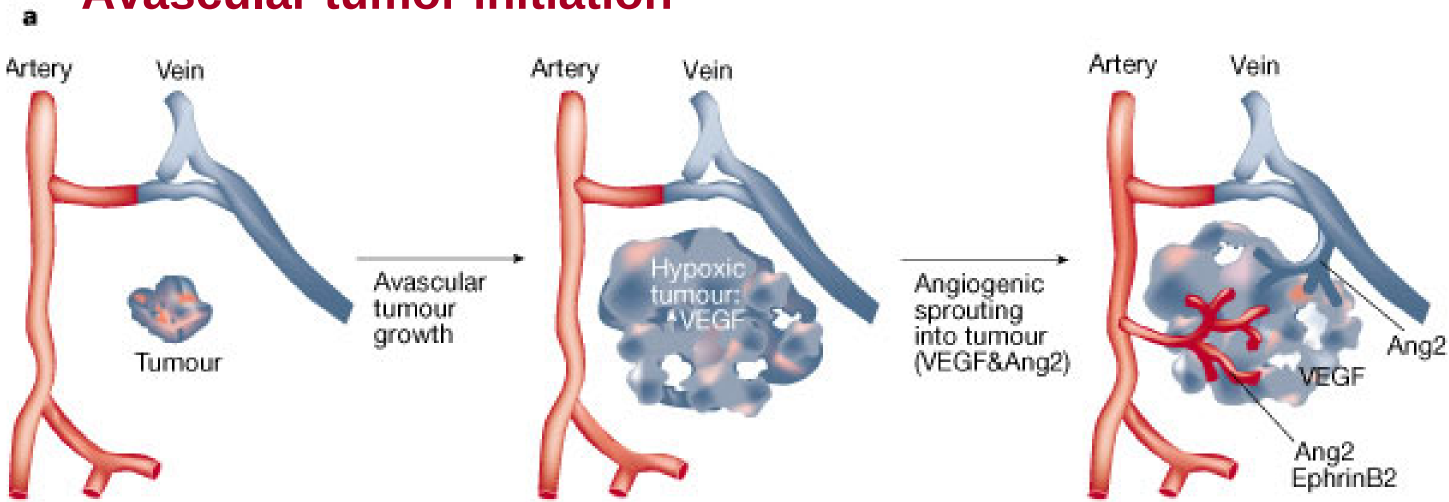
The capillary density depends on the tissue demand,
not on the limitations of a fractal supply network

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

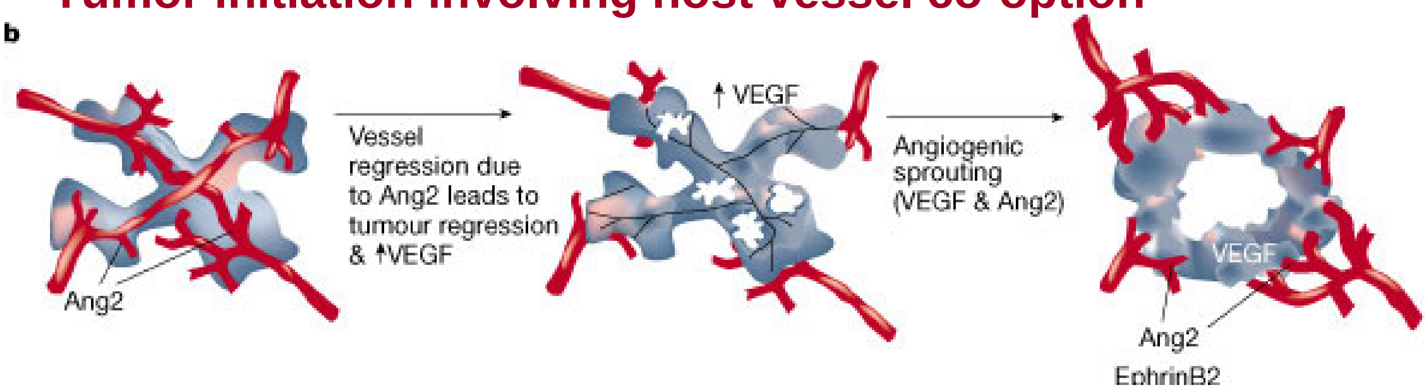


Models of tumour angiogenesis

Avascular tumor initiation



Tumor initiation involving host vessel co-option



High demand, high oxygen concentration

high flow, high RBC, high hemoglobin

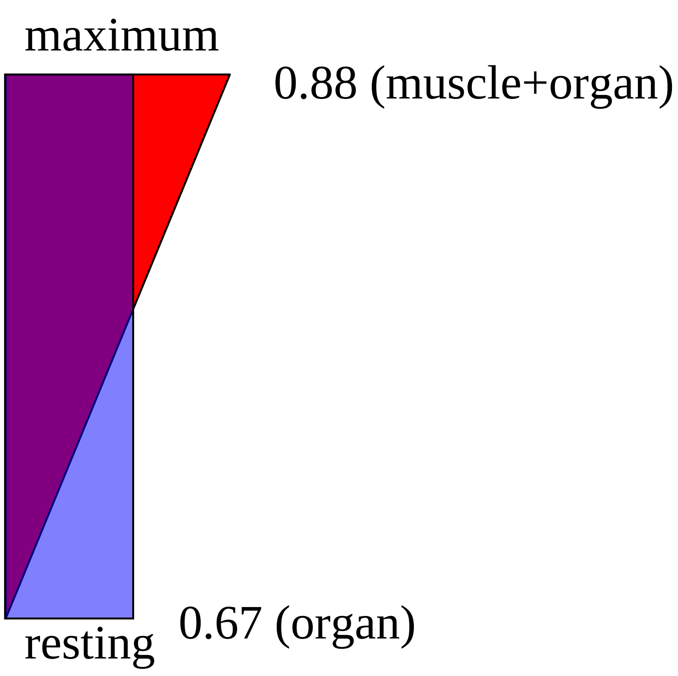
oxygen concentration in blood does not change (maybe toxic)

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

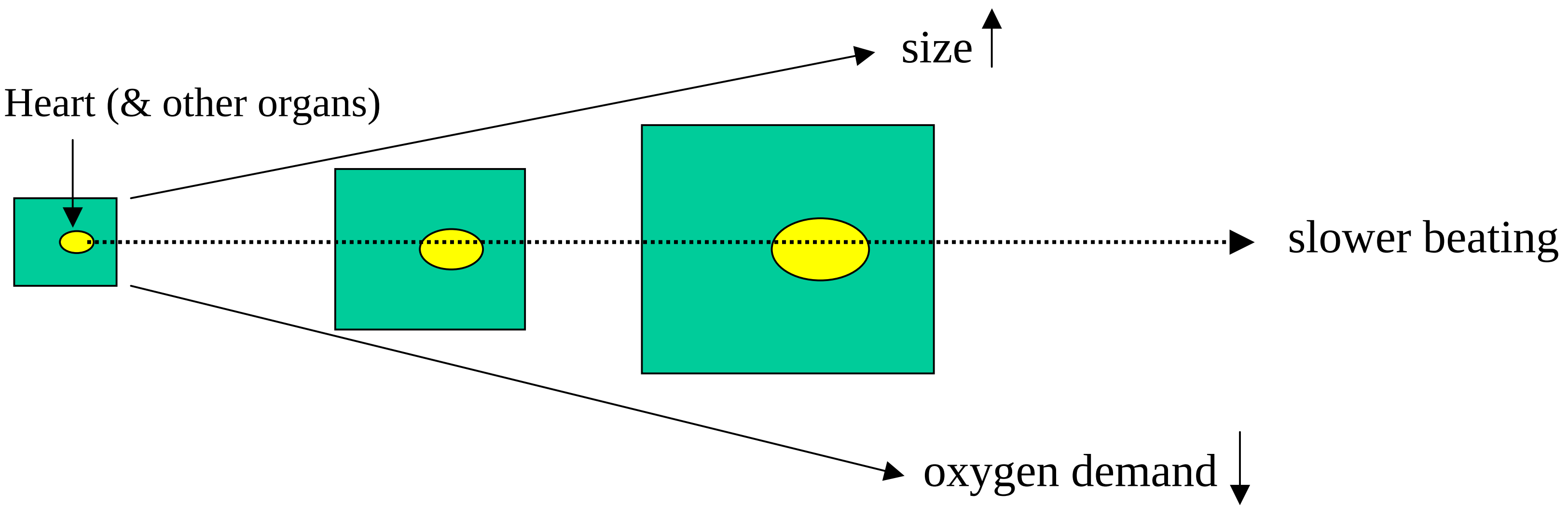
Part and parcel of metabolism

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?

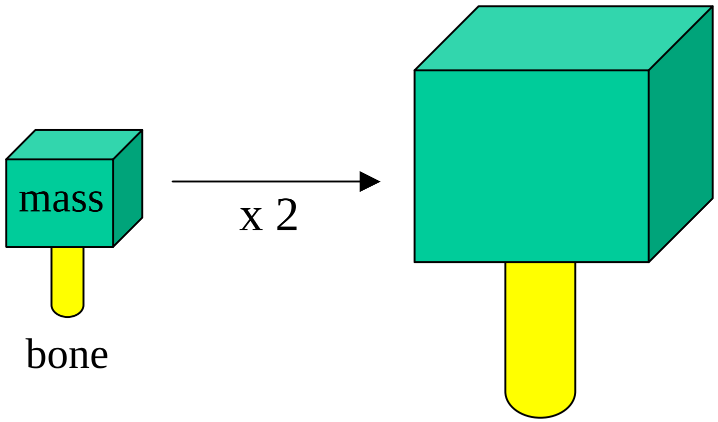


Heart contributes to resting metabolic rate
constant heart size relative to the body mass
but slower beating, because oxygen demand to other tissues has fallen
becomes faster, if demand increases

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:	1x1x1=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

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)
    - 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

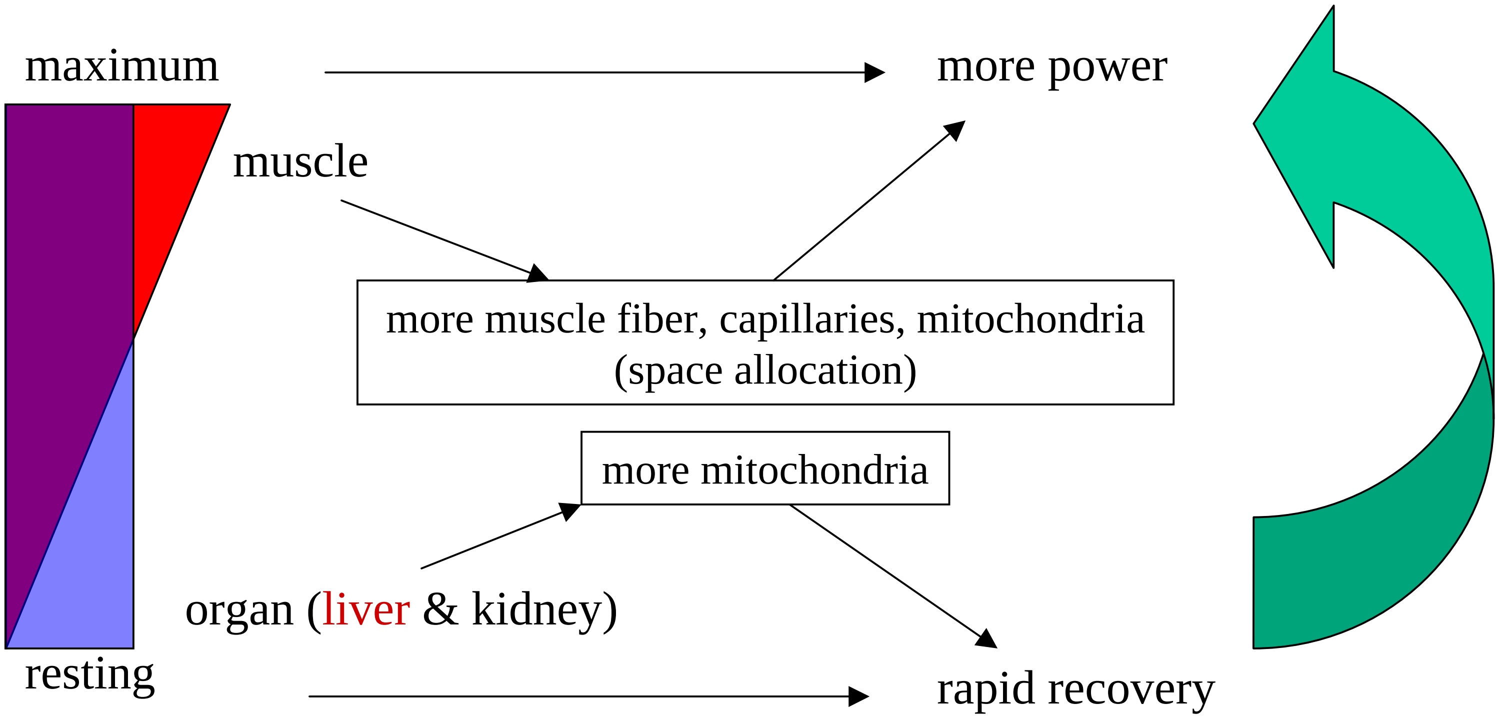
Sizing up to complexity

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

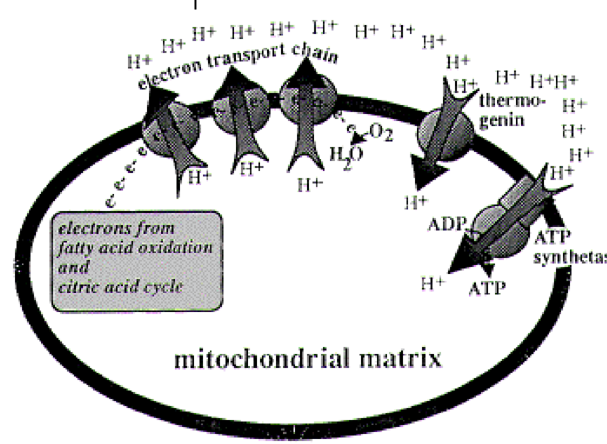


Proton leak

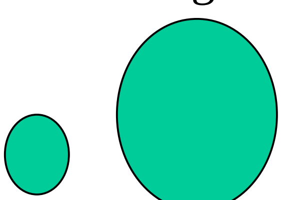
During rest diversion of blood flow from skeletal muscle to organs
Especially after a meal, blood is rich in nutrients

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



high surface area: high heat loss



Large animals:
metabolic power to balance muscular demand

Small animals:
metabolic power to maintain body temp

First lamp up the lamp

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
   economics of scale: energetic efficiency & modular system

2. How about single cells?
   intracellular modular system
   larger nucleus-larger DNA-raw material for complexity