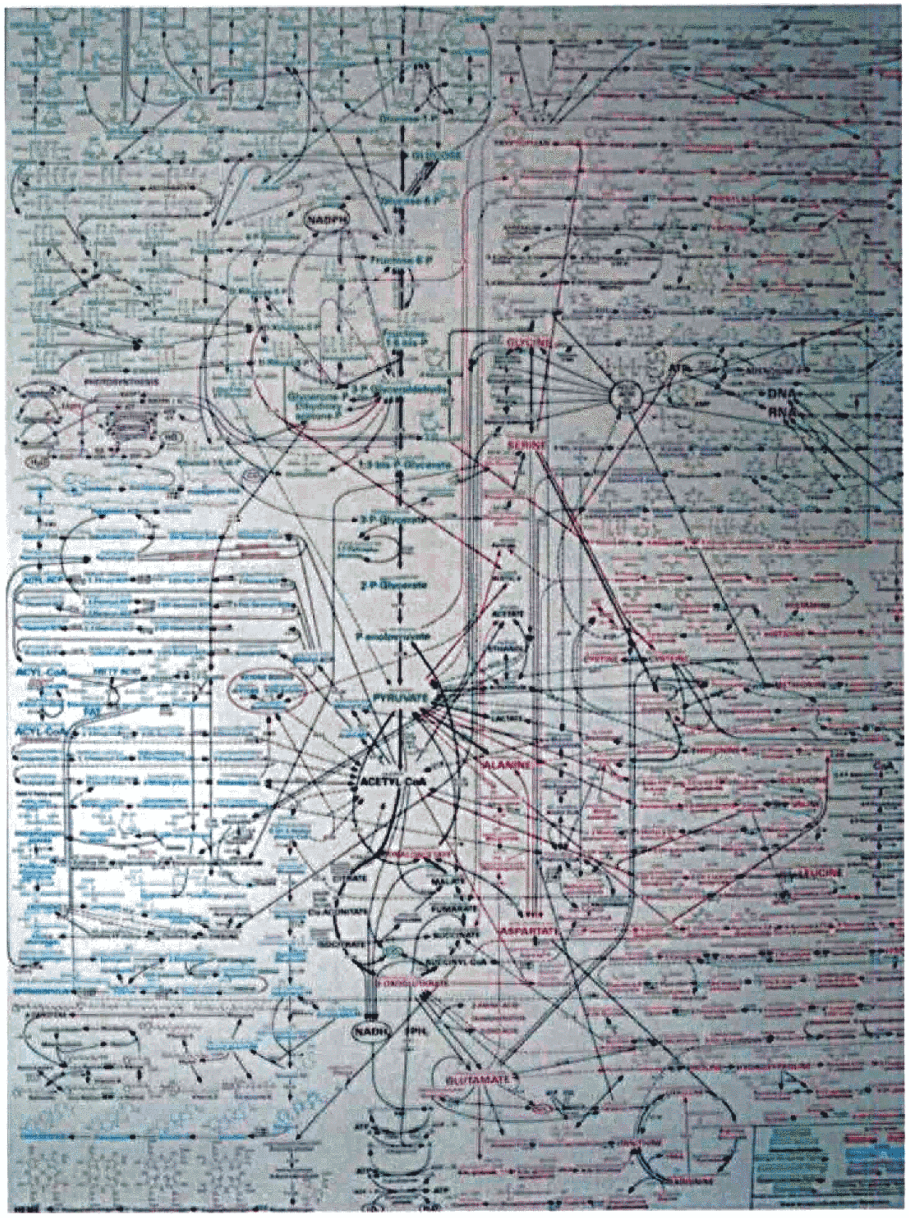


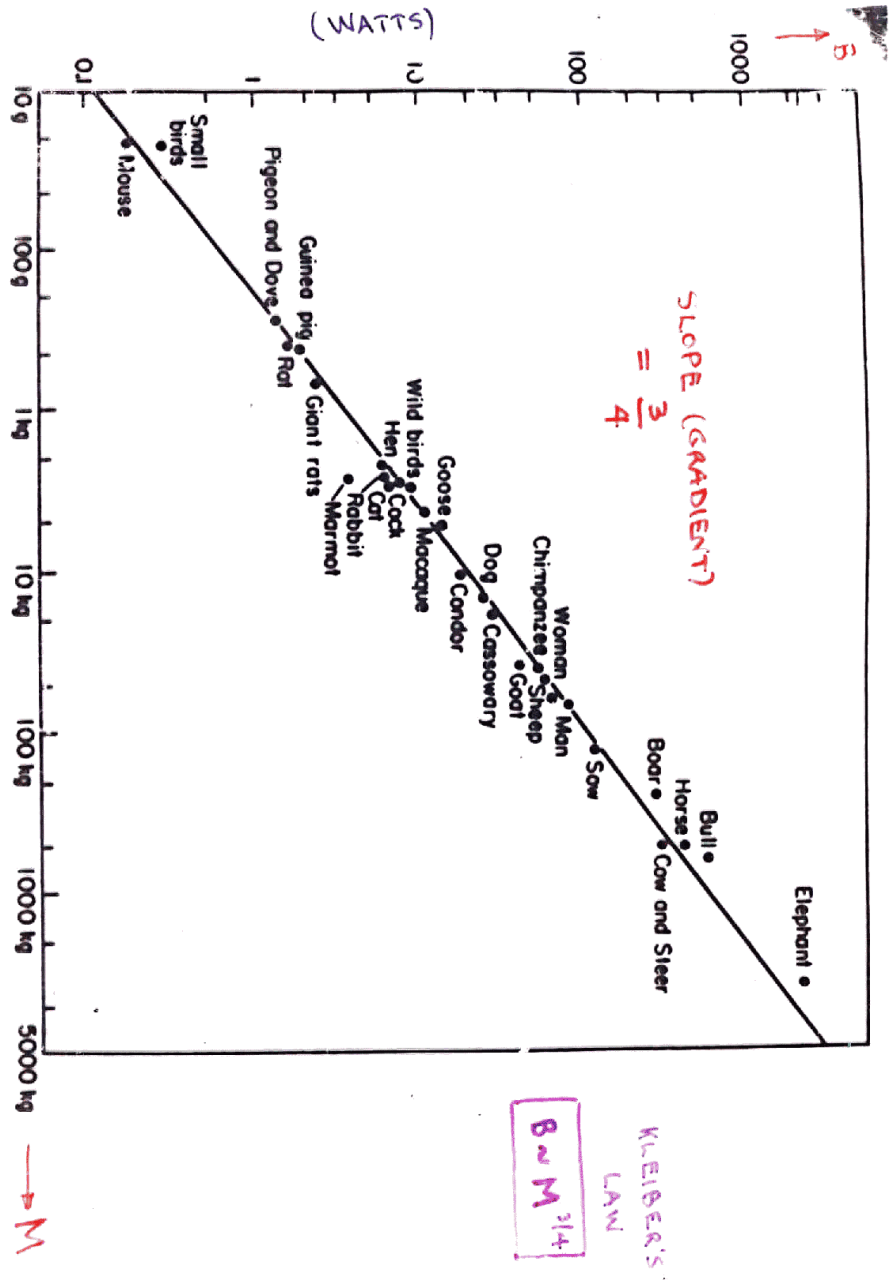


Fig. 4. Metabolic rates (in watts) of mammals and birds plotted on logarithmic coordinates against body mass (in kilograms).

METABOLIC RATE OF WHOLE ORGANISMS

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

TOTAL NUMBER OF CELLS IN ORGANISM $\propto M$

$\therefore$ METABOLIC RATE OF THE AVERAGE SINGLE CELL (IN VIVO)

$$B_c \propto \frac{B}{M} \propto \frac{M^{3/4}}{M} \propto \frac{1}{M^{1/4}}$$

[INCREASE MASS BY FACTOR OF $10^4 = 10{,}000$

THEN B INCREASES BY ONLY FACTOR OF $10^3 = 1{,}000$

SO $B_c \propto \frac{B}{M}$ DECREASES BY $\frac{1{,}000}{10{,}000} = \frac{1}{10}$]

$\Rightarrow$ METABOLIC RATE OF CELLS IN VIVO DECREASE WITH INCREASING BODY SIZE LIKE $\frac{1}{M^{1/4}}$

ANOTHER MANIFESTATION OF INCREASING EFFICIENCY AS SIZE INCREASES

IF $B \sim M^{3/4}$ THEN

METABOLIC RATE PER UNIT MASS

$$\frac{B}{M} \sim \frac{M^{3/4}}{M} \sim \frac{1}{M^{1/4}}$$

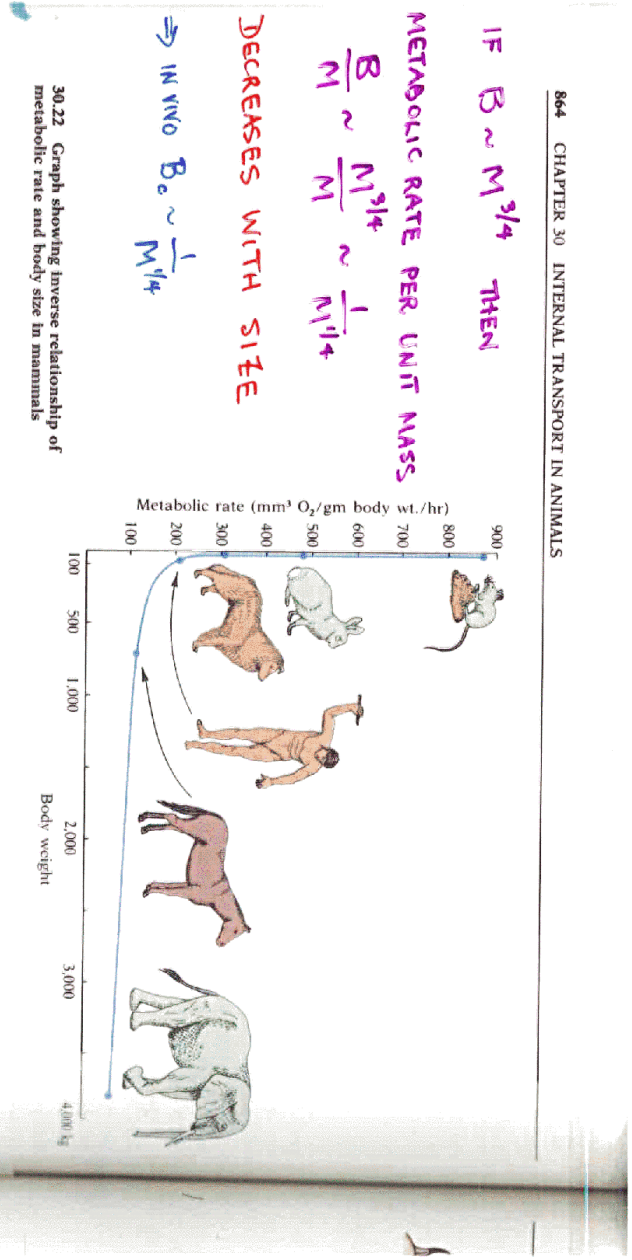
DECREASES WITH SIZE

$\Rightarrow$ IN VIVO $B_c \sim \frac{1}{M^{1/4}}$

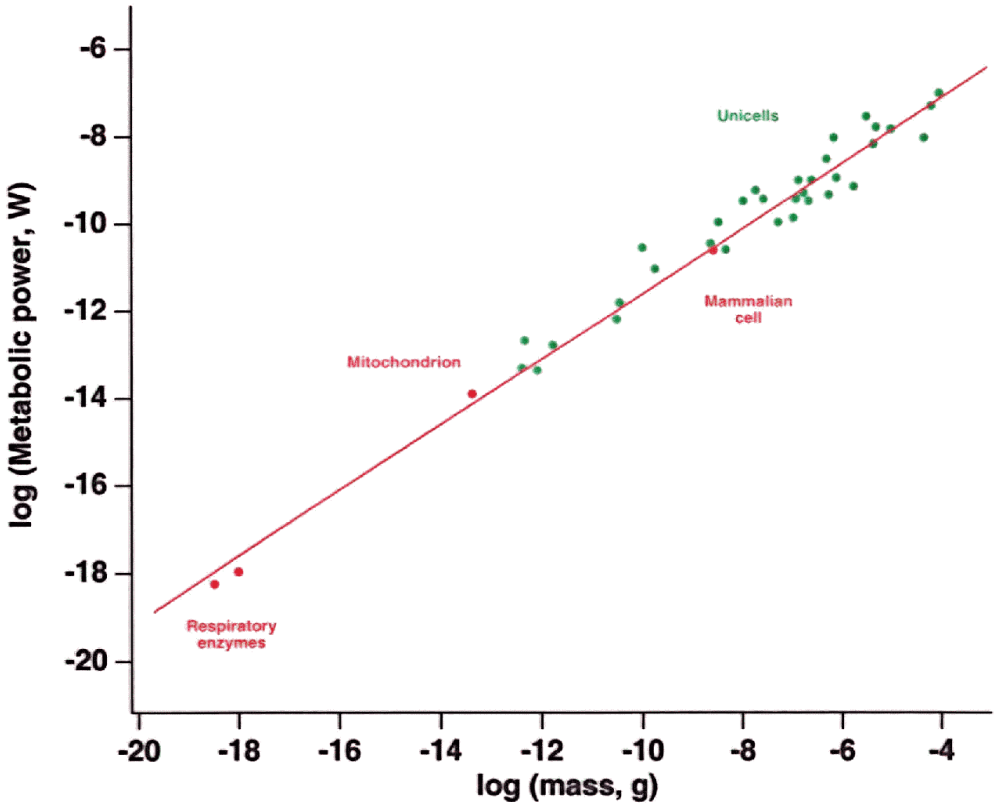
$\Rightarrow$ SMALL MAY BE BEAUTIFUL BUT LARGE IS MORE EFFICIENT

[CHEVRON + TEXACO → CHEVRON-TEXACO]

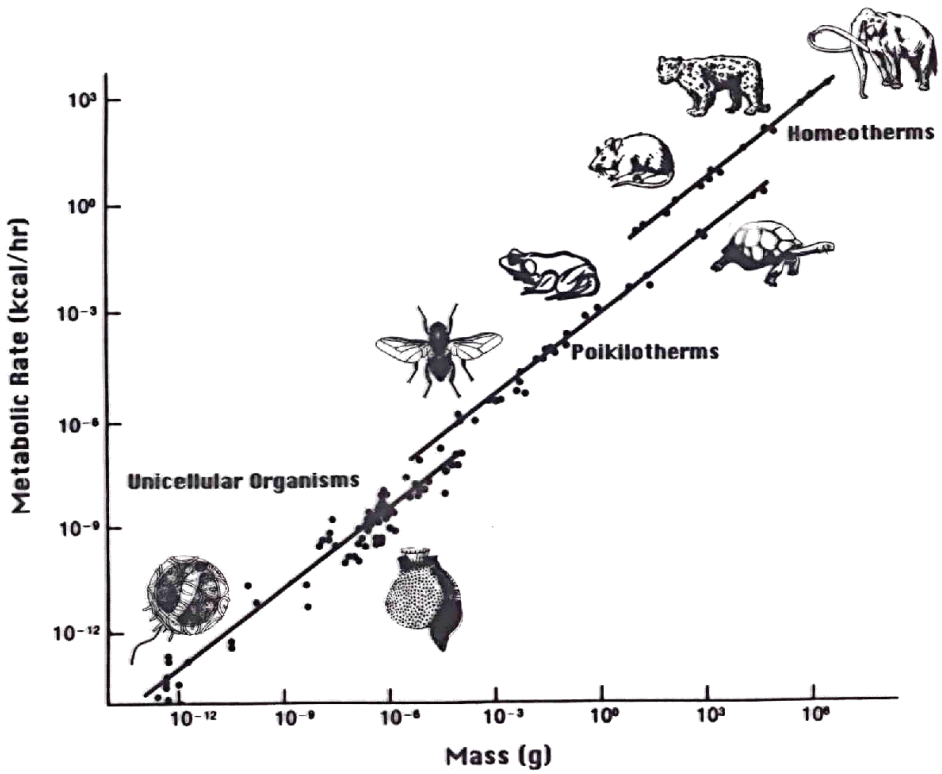
1 gm. OF MOUSE REQUIRES 3 TIMES THE POWER OF A DOG AND 9 TIMES THAT OF AN ELEPHANT !



30.22 Graph showing inverse relationship of metabolic rate and body size in mammals



HEMMINGSEN ~1950's



Allometric scaling of metabolic rate for a selection of homeotherms (birds and mammals), poikilotherms (fish, reptiles, amphibians, and invertebrates), and unicellular organisms. The solid lines all have a slope of .75. Modified from Hemmingsen, 1960.

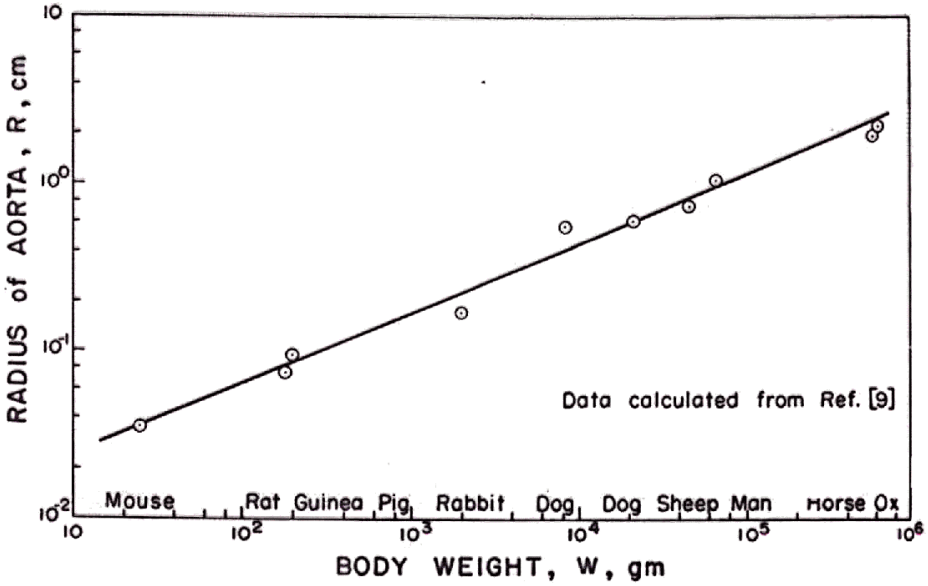
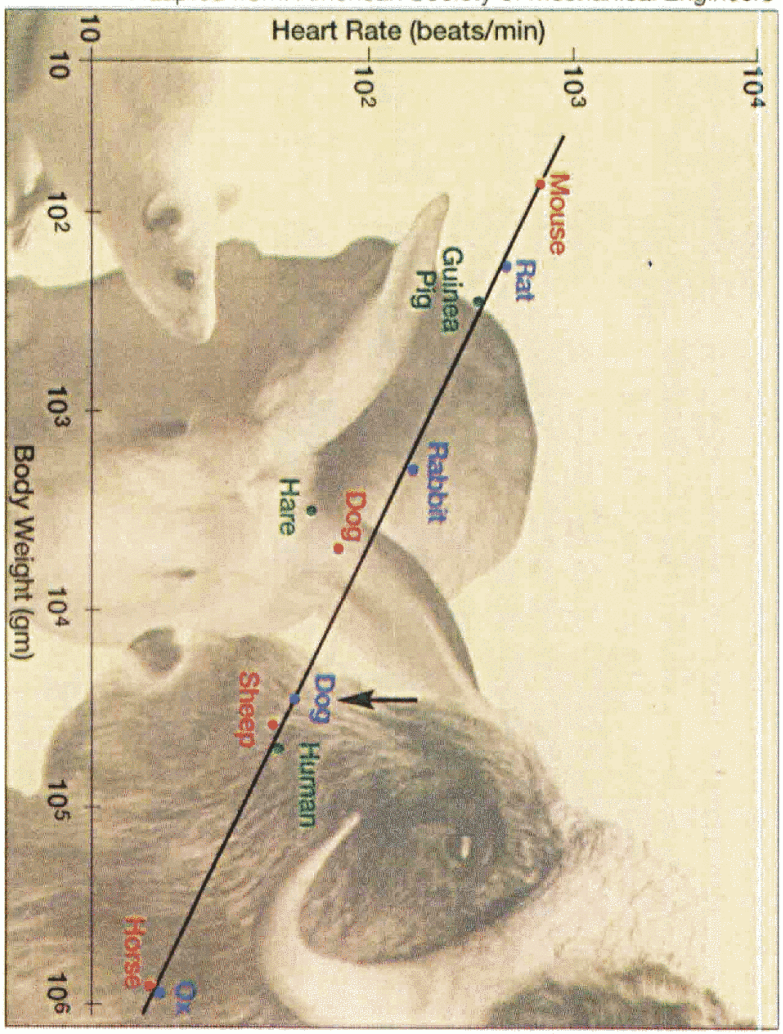


FIG. 4 – VARIATION IN RADIUS OF AORTA WITH BODY WEIGHT

$r \sim M^{3/8}$

SAME SCALING FOR TREE TRUNKS

Adapted from: American Society of Mechanical Engineers



Small mammals live fast and die young compared to big ones. Because heart rate tracks weight by a 1/4-power law, a dog (arrow) about 1/16 as heavy as a horse has a pulse about twice as fast as the horse's, not 16 times faster.

LIFESPAN

$$T \sim M^{1/4}$$

IF HEART-RATE (NUMBER OF BEATS PER SEC.)

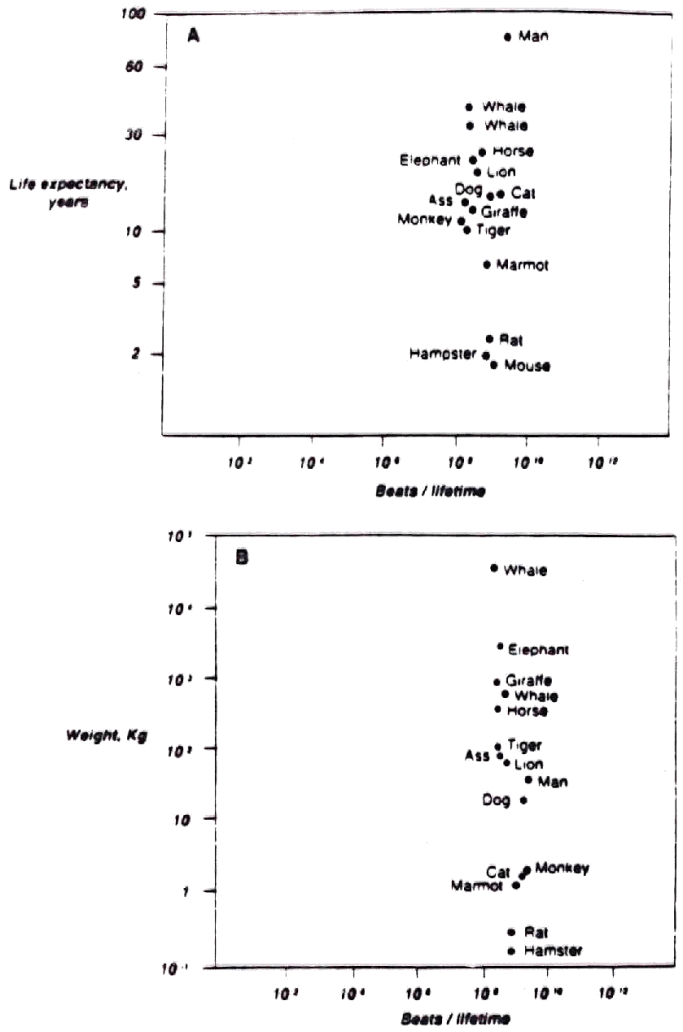
$$\sim M^{-1/4}$$

⇒ TOTAL NUMBER OF HEART-BEATS IN A TYPICAL LIFE-TIME IS INDEPENDENT OF SIZE!

$$\approx 1.5 \times 10^9$$

EACH ANIMAL SPECIES REGARDLESS OF SIZE HAS APPROXIMATELY THE SAME NUMBER OF HEART-BEATS IN ITS LIFE-TIME (ROUGHLY 1 BILLION)

[MORE FUNDAMENTALLY: SAME NUMBER OF TURNOVERS OF CytO ENZYME IN ITS RESPIRATORY COMPLEX PER LIFESPAN $\sim 10^{16}$]



ANOTHER INVARIANT :

RECALL SPECIFIC METABOLIC RATE

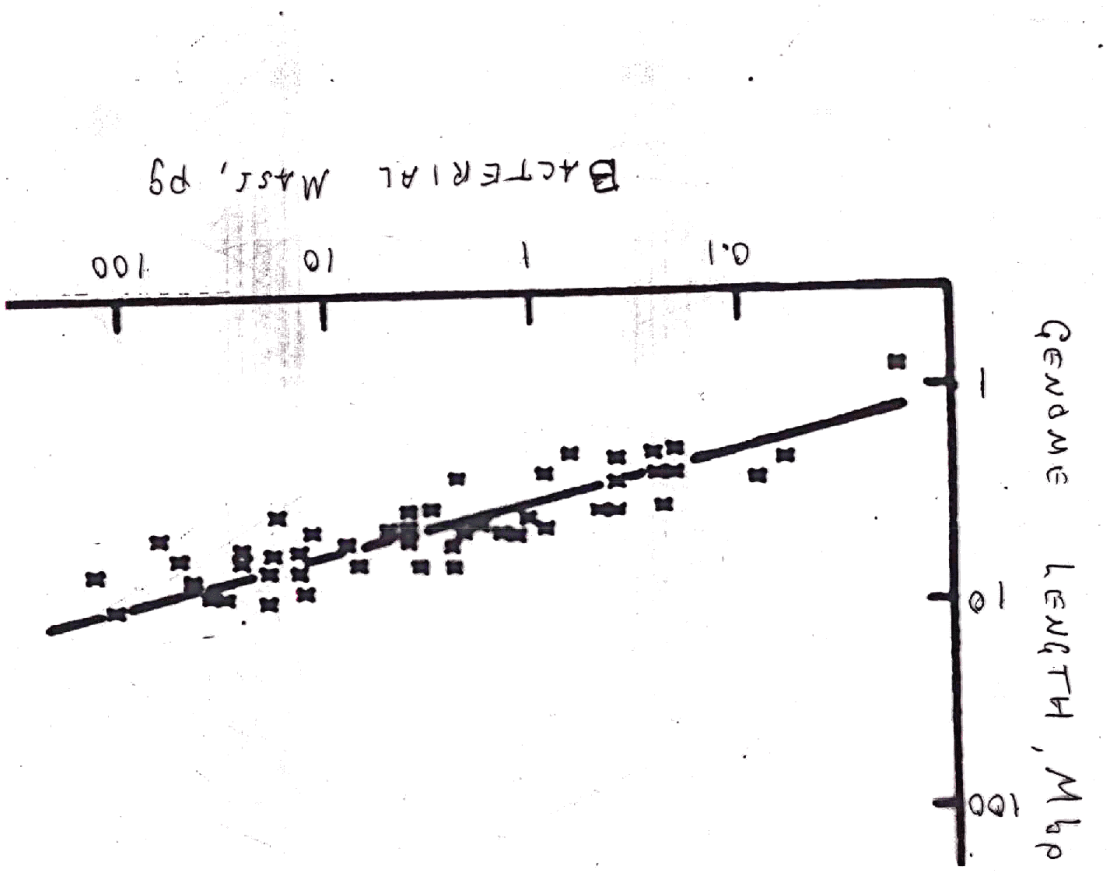
$$\bar{B} = \frac{B}{M} \propto M^{-1/4}$$

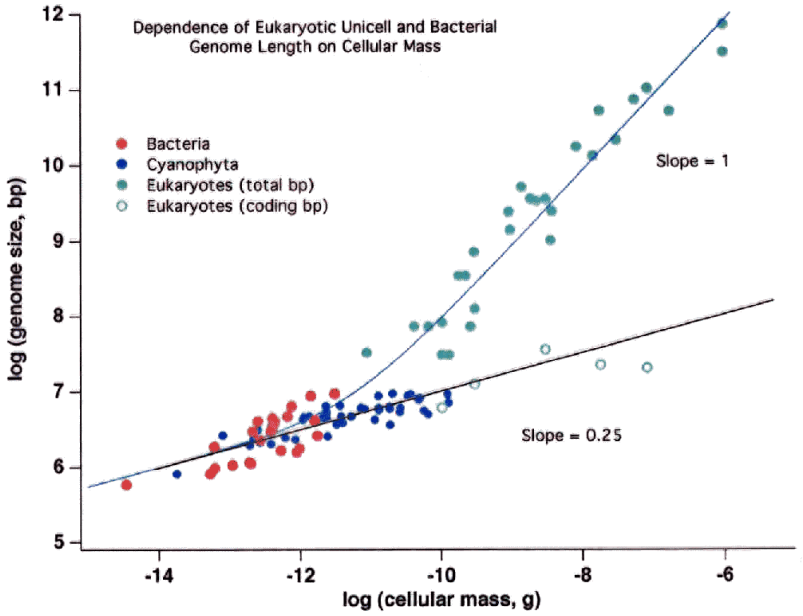
$\Rightarrow$ TOTAL ENERGY NEEDED TO SUPPORT UNIT MASS OF AN ANIMAL DURING A LIFETIME IS THE SAME FOR ALL ANIMALS REGARDLESS OF SIZE :

$$E_{TOT} \approx 1.2 \times 10^{6} \text{ JOULES / gm}$$

$$\approx 300 \text{ Kcals / gm}$$

$$\approx 5.2 \text{ moles } O_2 \text{ / gm}$$





- **Prokaryotic Genome Length is Adapted to Cellular Energetics: Average Copy Number of Gene Products Predicted to Scale as M**0.75**
- **Size and Numerical Distribution of Prokaryotes in an Ecosystem Yields: "Metagenome" Parameters Energy Flux of the Ecosystem, Total and Individual Organisms**
- **Coding Genome Length of Eukaryotes May Follow "Prokaryote Law", thus: Total Ecosystem Functional Diversity May Be Predictable**

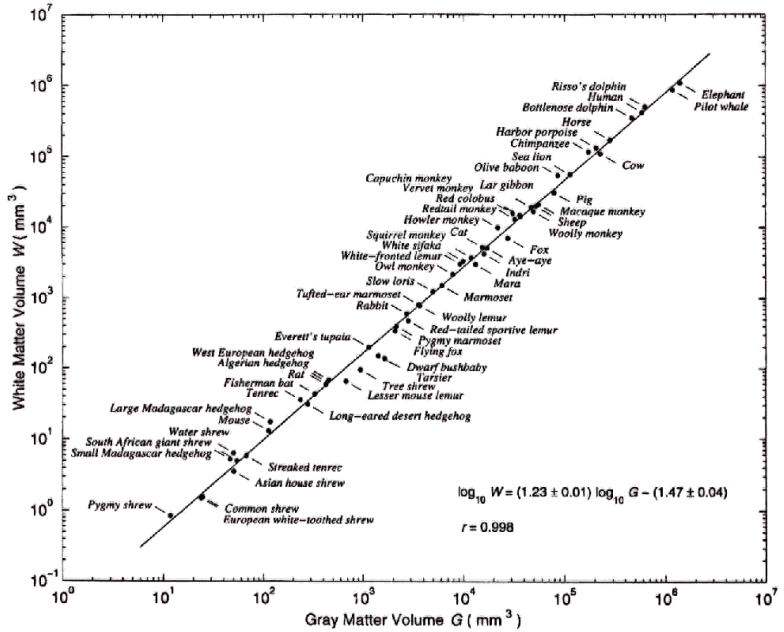


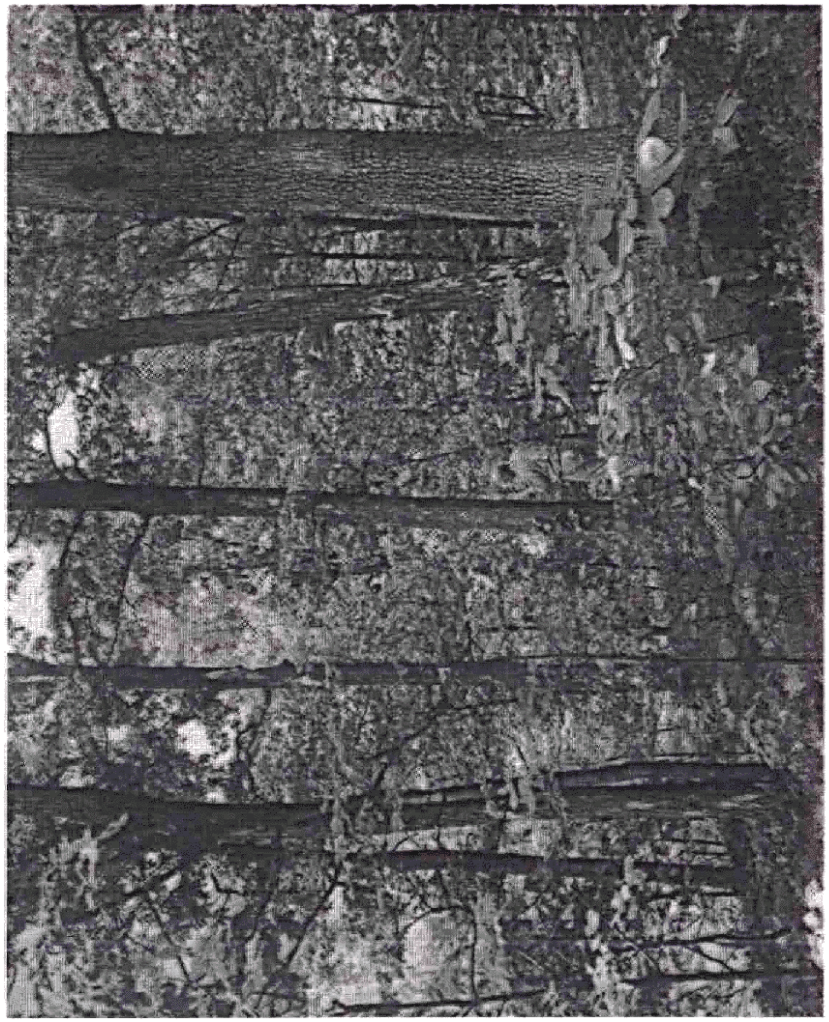
Fig. 2. Cortical white and gray matter volumes of various species ($n = 59$) are related by a power law that spans five to six orders of magnitude. Most data points are based on measurement of a single adult animal. The line is the least squares fit, with a slope around 1.23 ± 0.01 (mean ± SD). The average and median deviations of the white matter volumes from the regression line are, respectively, 18% and 13% on a linear scale. *Sources of data:* If the same species appeared in more than one source below, the one mentioned earlier was used. All 38 species in table 2 in ref. 3 were taken, including 23 primates, 2 tree shrews, and 13 insectivores. Another 11 species were taken from table 2 in ref. 8, including 3 primates, 2 carnivores, 4 ungulates, and 2 rodents. Five additional species came from table 1 in ref. 11, including 1 elephant and 4 cetaceans. The data point for the mouse ($G = 112$ mm^3 and $W = 13$ mm^3) was based on ref. 30, and that for the rat ($G = 425$ mm^3 and $W = 59$ mm^3) was measured from the serial sections in a stereotaxic atlas (42). The estimates for the fisherman bat (*Noctilio leporinus*, $G = 329$ mm^3 and $W = 43$ mm^3) and the flying fox (*Pteropus lylei*, $G = 2{,}083$ mm^3 and $W = 341$ mm^3) were based on refs. 43 and 44, with the ratios of white and gray matters estimated roughly from the section photographs in the papers. The sea lion data (*Zalophus californianus*, $G = 113{,}200$ mm^3 and $W = 56{,}100$ mm^3) were measured from the serial sections at the website given in the legend to Fig. 1, with shrinkage correction.

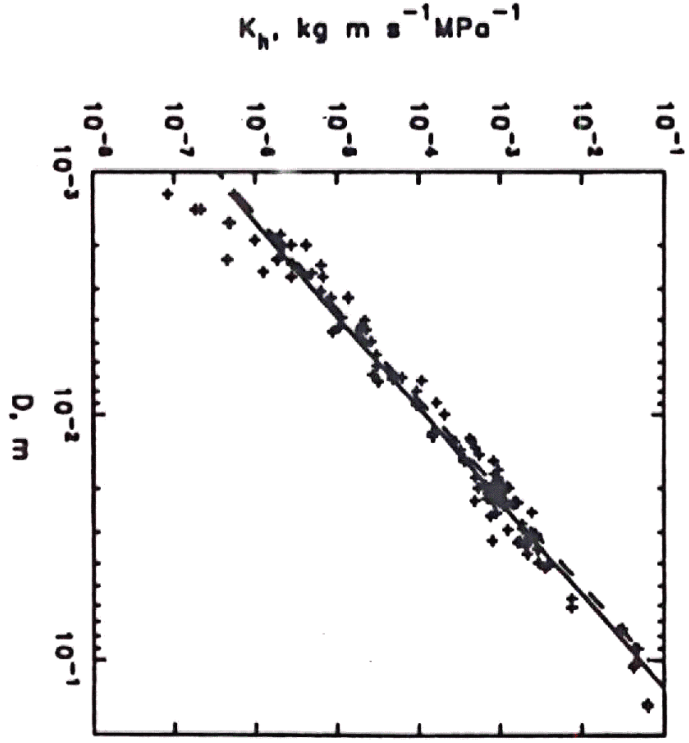
squares of perpendicular distance, and least absolute deviations, the third of which is more robust against outliers (13). The standard deviations for the slope and intercept were estimated directly for the first method and by bootstrap for the last two methods (14). Bootstrap may help detect outliers in the data because, when they are left out from a same-size resample, the correlation coefficient often increases, which could be exploited to improve estimation. Systematic bias caused by outliers was not detected in Fig. 2.

3. Theory of Scaling

Our analysis rests on two assumptions. First, we assume that each small piece of cortex of unit area, regardless of its thickness and the overall brain size, sends and receives about the same total cross-sectional area of long-distance connection fibers to and from other cortical regions. Second, we assume that the global geometry of the cortex minimizes the average length of the long-distance fibers.

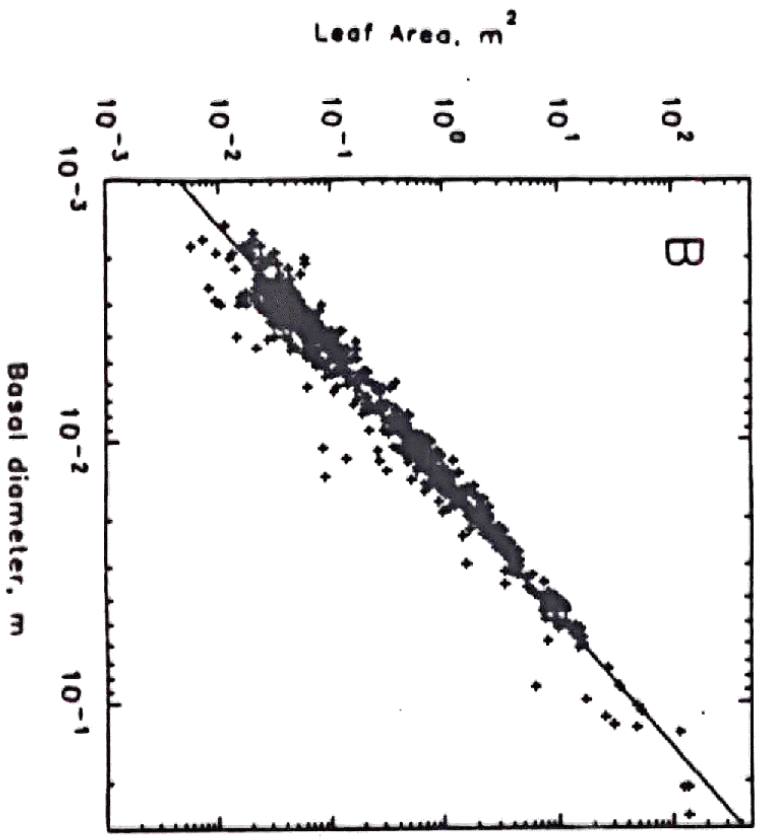
The second assumption follows from Ramon y Cajal's principle for conservation of space, conduction time, and cellular materials (Chap. V in ref. 15). This principle has been explored more recently as the principle of minimal axon length (16–18). Consistent with previous observations on the basic uniformity of the cortex (19–21), the first assumption is supported loosely by the evidence that the total number of neurons beneath a unit cortical surface area is about 10^5/mm^2 across different cortical regions for several species, from mouse to human (22) (after shrinkage correction). But there are exceptions, including the higher density in striate cortex of primates (22, 23), the lower density in dolphin cortex (24), and the variability observed in cat cortex (25). The number of axons leaving or entering the gray–white boundary per unit cortical area should be compara-



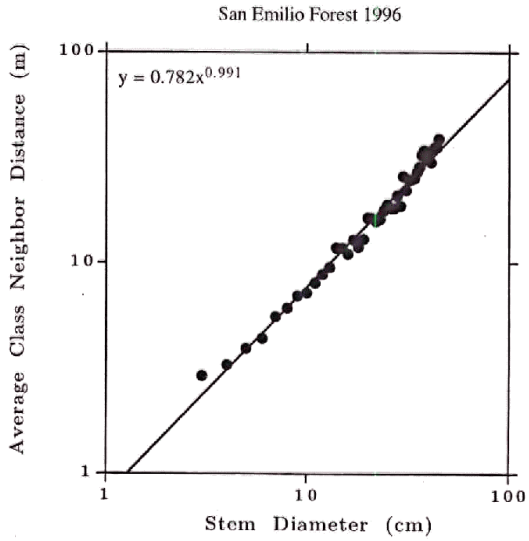


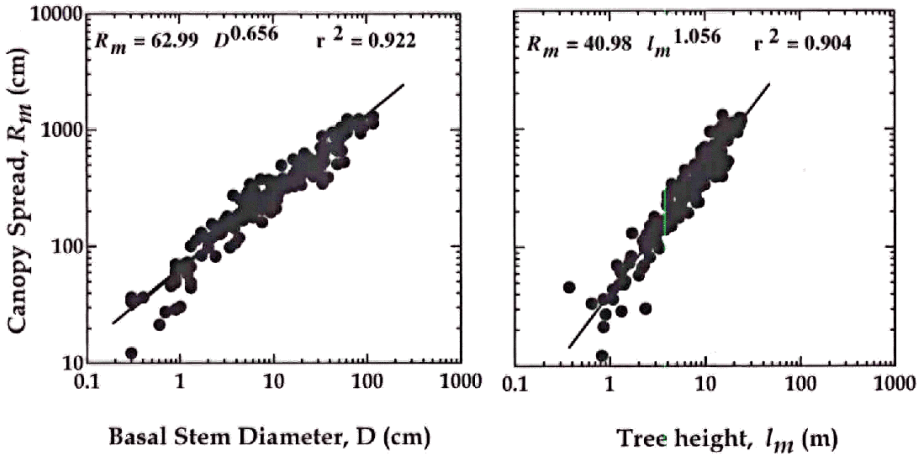
$K_h \propto D_h^{2.64}$

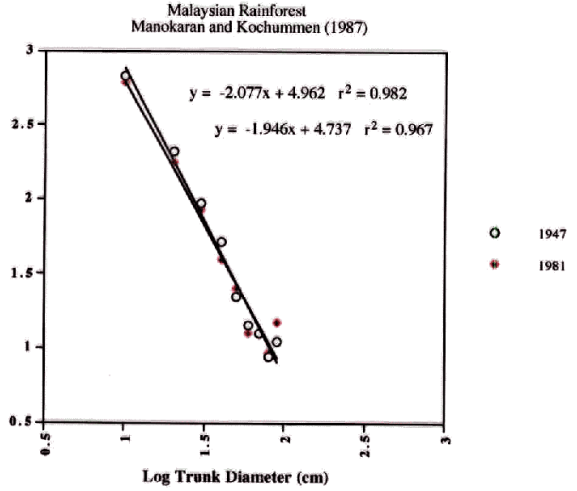
PREDICT $K_h \propto D_h^{8/3 = 2.67}$

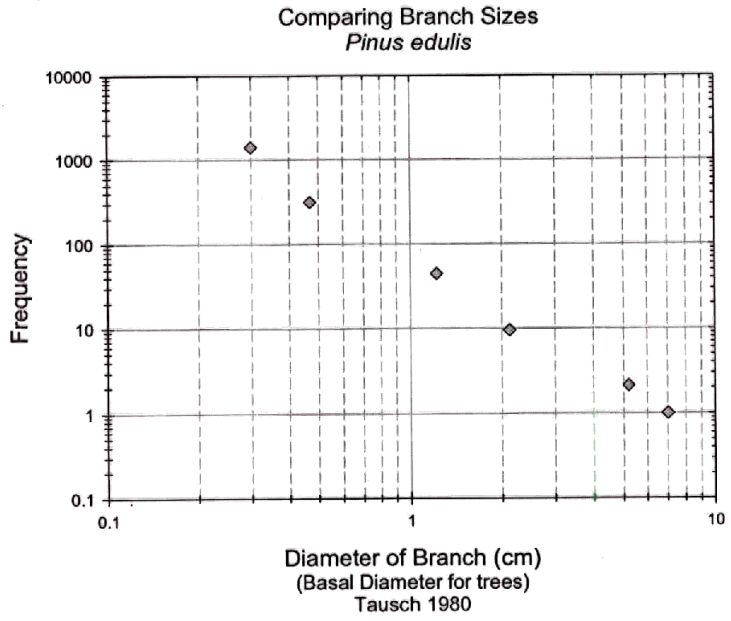


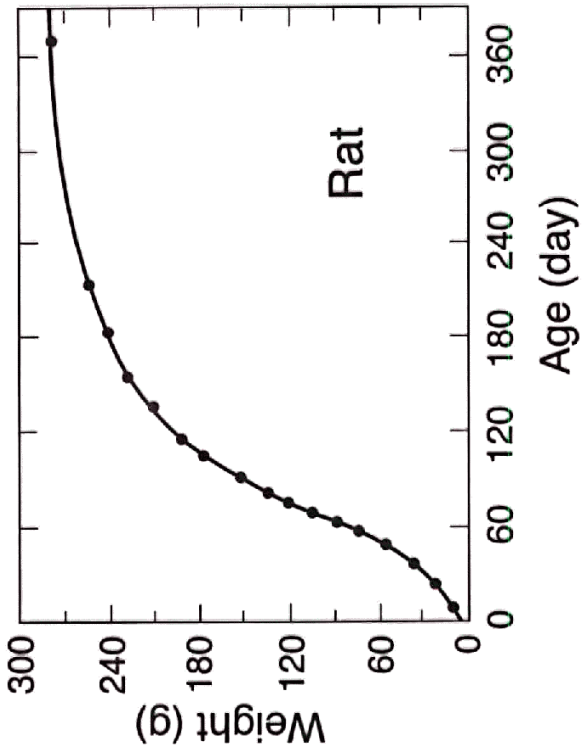
$A_k^L = 1.17 \times 10^4 \tau_k^2$

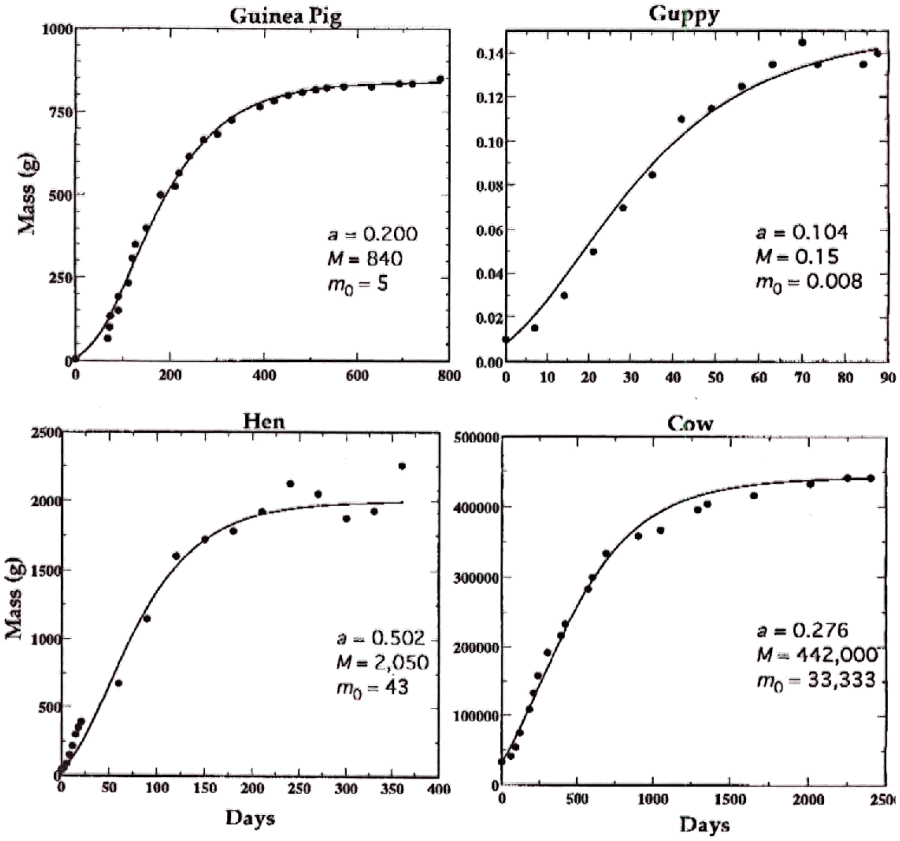



$R_m = 62.99\ D^{0.656}$ r 2 = 0.922
$R_m = 40.98\ l_m^{1.056}$ r 2 = 0.904
Canopy Spread, R_m (cm)
10000
1000
100
10
0.1
1
10
100
1000
Basal Stem Diameter, D (cm)
Tree height, l_m (m)

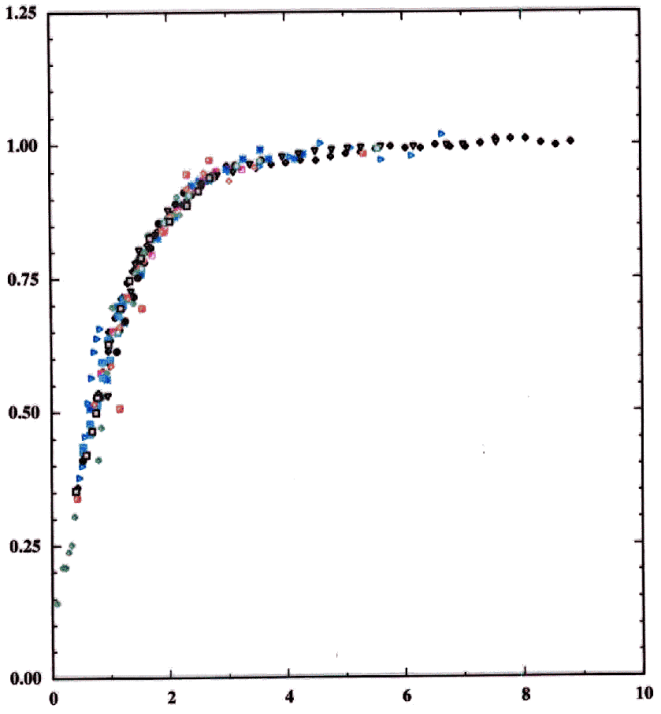

Malaysian Rainforest
Manokaran and Kochummen (1987)
y = -2.077x + 4.962 r2 = 0.982
y = -1.946x + 4.737 r2 = 0.967
1947
1981
Log Trunk Diameter (cm)


Comparing Branch Sizes
Pinus edulis
Frequency
10000
1000
100
10
1
0.1
0.1
1
10
Diameter of Branch (cm)
(Basal Diameter for trees)
Tausch 1980


Rat
Weight (g)
300
240
180
120
60
0
0
60
120
180
240
300
360
Age (day)

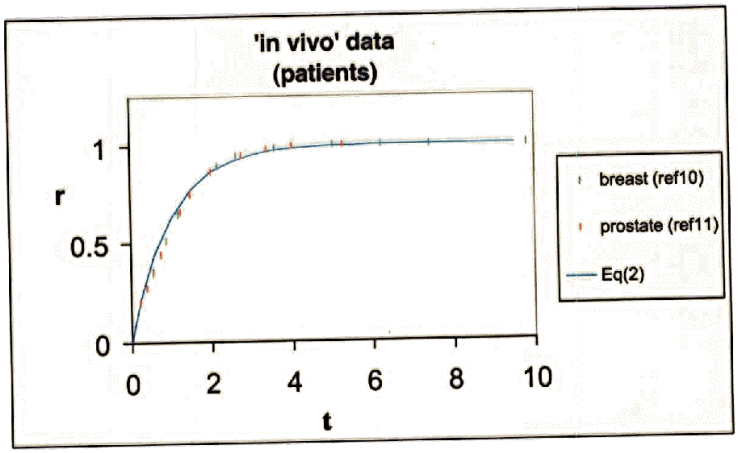


$\gamma = (m/M)^{1/4} = \frac{\text{ENERGY FOR MAINTENANCE}}{\text{TOTAL METABOLIC ENERGY}}$

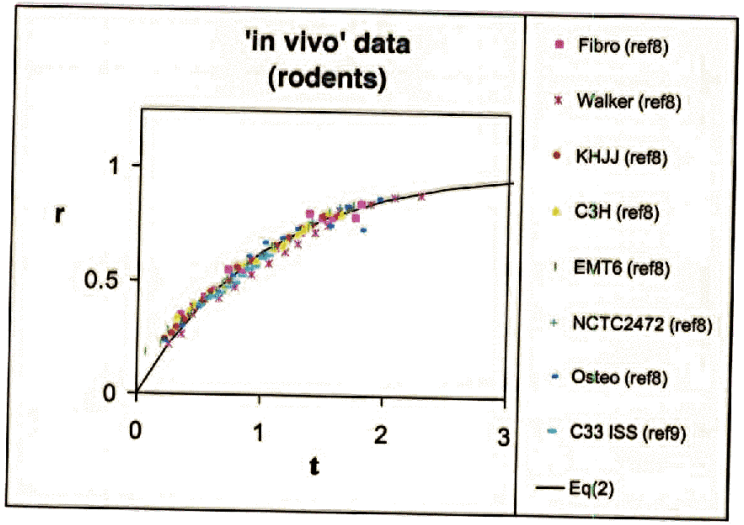


$\frac{B_0 M_c}{E_c}$

GUIOT et al 2003



14



13

(9)

WHEN SIZE EVOLVES TO $M \gtrsim \mu$ DRAMATIC INCREASE IN EFFICIENCY BY PULSATILE FLOW

SUGGEST NO MAMMAL WITH $M \lesssim \mu$ CAN EXIST

b) CALCULATION OF μ

HAD FOR THE CROSS-OVER FROM PULSATILE TO NON-PULSATILE

$$\frac{\tau^2}{\ell} \approx \frac{8\nu}{\rho c_0} \quad \leftarrow \text{VISCOSITY}$$

$$\left(\frac{Eh}{2\rho r}\right)^{1/2} \sim 600\,\text{cm/sec}$$

ABSOLUTE MINIMUM VALUE IS THE MASS WHERE τ AND ℓ CORRESPOND TO THE AORTA

BUT, HAD $\tau \sim M^{3/8}$ AND $\ell \sim M^{1/4}$

SO $\frac{\tau^2}{\ell} \sim M^{1/2}$

$$\Rightarrow \mu \approx M \left(\frac{8\nu}{\rho c_0} \frac{\ell_0}{\tau_0^2}\right)^2$$

↑ LENGTH AND RADIUS OF AORTA OF A MAMMAL OF MASS M

$\rho \approx 1\,\text{gm/c.c.}$
$\nu = 0.04$ poise
$M = 10\,\text{Kg}$
$\Rightarrow \mu \sim 3\,\text{gm}$

(10)

$$\Rightarrow \frac{\text{MITO. VOLUME}}{\text{BODY VOLUME}} \approx \frac{N_m^0 M_m}{M}$$

$$= \left(\frac{\mu M_m}{M_c M}\right)^{1/4}$$

$$\approx 0.06\, M^{-1/4} \qquad (M \text{ IN gms.})$$

(DATA → $0.07\, M^{-1/4}$)

$M_c \approx 3\times10^{-9}$ gm
$M_m \approx 4\times10^{-14}$ gm
$M = 50$Kg
$\mu \sim 1$ gm

$N_m^c \sim 300$ (IN VIVO)

AT $M = \mu$

$$N_m^c = \left(\frac{M_c}{M_m}\right)^{3/4}$$

$\approx$ 5000 (IN VITRO)

CAN EXTEND TO RESP. COMPLEXES:

$$B(M, M_c, M_m, M_r) = N_r^0 B_r$$

↑ NUMBER OF RC's IN ORGANISM

$$N_r^0 = N_r^m N_m^c N_c^0$$

$$\Rightarrow \text{DENSITY } \rho_r^0 = \frac{N_r^0}{M} = \left(\frac{\mu}{M_c M_r^3 M}\right)^{1/4} \propto M^{-1/4}$$

$M_r \approx 1\times10^{-18}$ gm $\Rightarrow N_r^m \approx \left(\frac{M_m}{M_r}\right)^{3/4} \approx 3000$ INDEPENDENT OF M

FUNDAMENTAL PRINCIPLES (NATURAL SELECTION)

I. AT ALL SCALES ORGANISMS ARE SUSTAINED BY THE TRANSPORT OF ENERGY AND ESSENTIAL MATERIALS THROUGH HIERARCHICAL BRANCHING NETWORK SYSTEMS IN ORDER TO SUPPLY ALL LOCAL PARTS OF THE ORGANISM

II. THESE NETWORKS ARE SPACE-FILLING

III. THE TERMINAL BRANCHES OF THE NETWORK ARE INVARIANT UNITS

IV. ORGANISMS HAVE EVOLVED BY NATURAL SELECTION SO AS TO

i) MINIMISE ENERGY DISSIPATED IN THE NETWORKS

AND/OR ii) MAXIMISE THE SCALING OF THEIR AREA OF INTERFACE WITH THEIR RESOURCE ENVIRONMENT

LIFE IS THE MOST COMPLEX SYSTEM

SCALING LAWS ARE REMARKABLE BECAUSE

i) THEY EXIST

ii) THEY ARE VERY SIMPLE } DOMINANCE OF 1/4 POWER

iii) THEY ARE UNIVERSAL

iv) ⇒ BIGGER IS MORE EFFICIENT

v) FEW QUANTITATIVE "LAWS" IN BIOLOGY

"EVERYTHING" IS DERIVED FROM THESE BASIC PRINCIPLES

IN PARTICULAR, SCALING AND THEIR EXPONENTS ARISE FROM AN INTERPLAY BETWEEN THE PHYSICAL AND GEOMETRICAL CONSTRAINTS INHERENT IN THESE PRINCIPLES

EXAMPLES

CARDIOVASCULAR/CIRCULATORY SYSTEM

RESPIRATORY SYSTEM

RENAL SYSTEM

NEURAL SYSTEM

PLANT/TREE VASCULAR SYSTEM

⋮

CITY WATER SUPPLY

? COMPUTER NETWORKS
RIVERS
CORPORATE STRUCTURES

JIM BROWN, REGENTS' PROF. OF BIOLOGY, UNM

BRIAN ENQUIST, UNIV. OF ARIZONA

WOODY WOODRUFF, LANL

RIC CHARNOV, UNM

JAMIE GILLOOLY, UNM POST-DOC

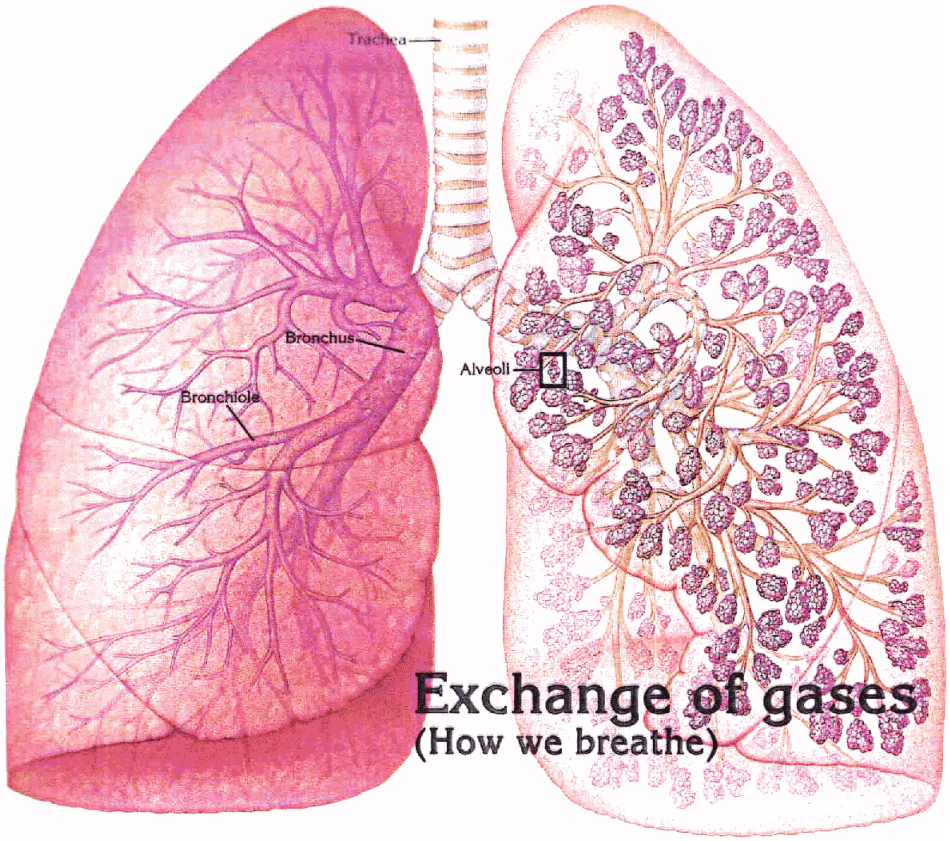
VAN SAVAGE, SFI & LANL POST-DOC

DREW ALLEN, STUDENT UNM

SCIENCE
NATURE
PNAS

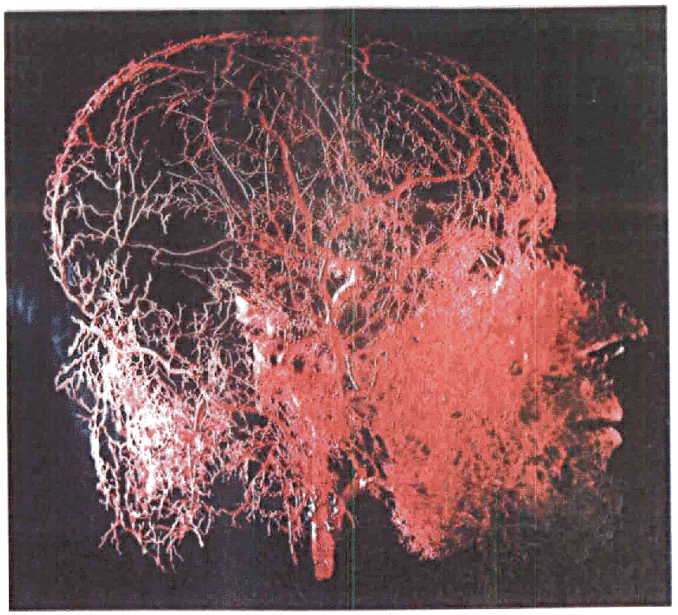
DOE
NSF
PACKARD FOUNDATION
THAW CHARITABLE TRUST
LDRD !!

1 cm



rbed
owly
orm
into
near

hose
mph
hose
f the
anti-
ntra-
ly be
ı the
mph
ns to
ı the
mph
fluid
en it
ıid is
.19).
ning



30.18 Blood vascular network in the human head The human face, particularly the area around the lips, contains a dense array of capillaries.

30.13 Blood vessels and capillaries
Left: The vessels in the web of a living frog's foot branch repeatedly. The smallest capillaries (seen here as very thin, faintly red lines) reach all cells. Right: In this longitudinal section of a human capillary, individual erythrocytes are seen moving single file.

muscle tissue con
of cross section.
dom much larger
them (Fig. 30.13).
vidual capillaries
sure not only that
but also that a ver
change process. It
contacts nearly o
through a capillar
total cross-sectior
slowly in the capil
flow allows more

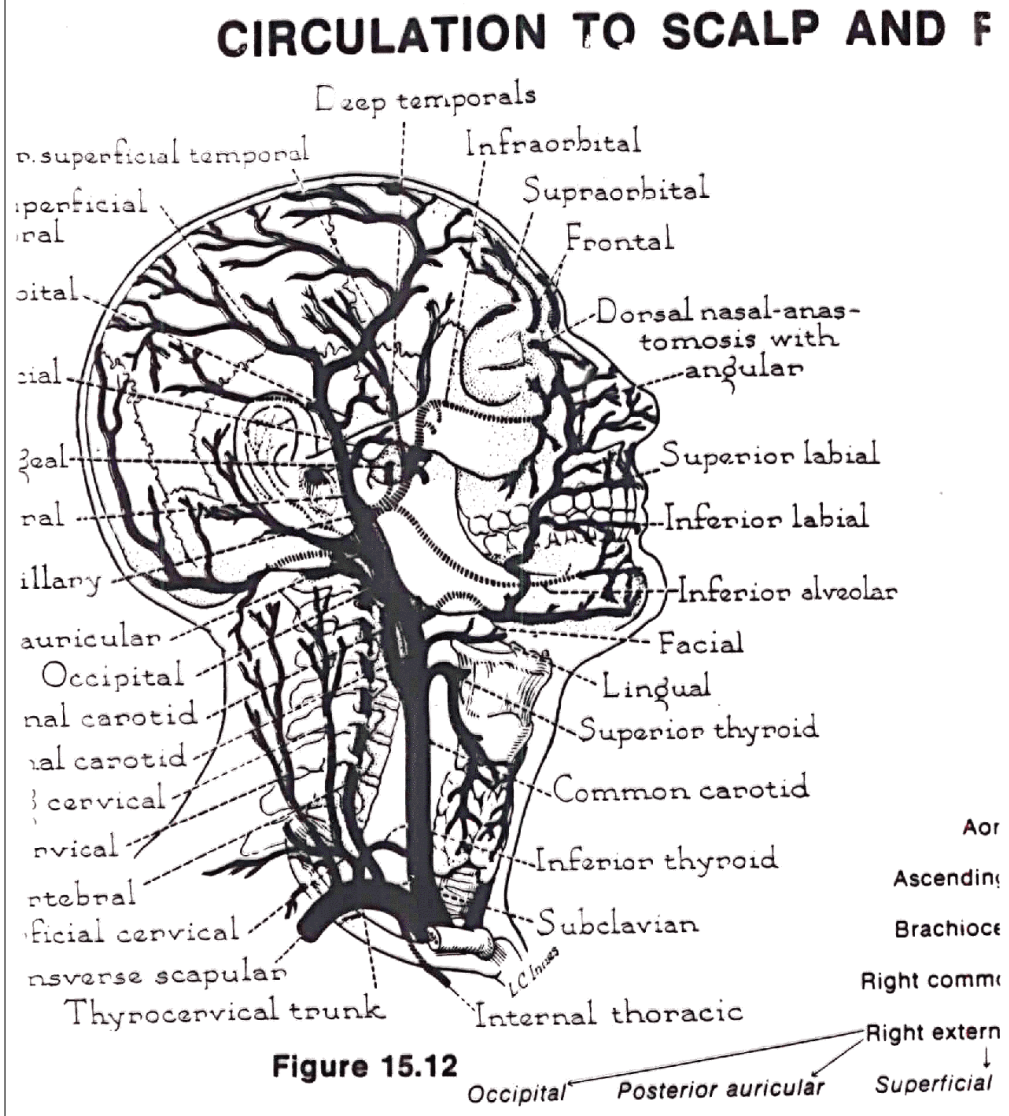


Figure 15.12

an adult cerebellum (Figure 5), is the tree-like structure, with white matter penetration minimizing the distance to the cortical surface in an efficient manner while preserving a significant perimeter-to-length relationship.

5.2 BRONCHIAL AIRWAY

The morphology of the bronchial airway has features that lend themselves to fractal analysis. The fetal bronchial tree develops *in utero* prior to any requirement for oxygen transport. In contrast to other developing organs, the architectural development of the bronchial tree is dependent only on external constraints provided by the chest cavity and diaphragm for its final geometry; suggesting that airway morphology is the result of an evolutionary process with structural characteristics transmitted via the gene pool (Figure 6). The geometry of the lung is remarkably consistent between individuals; however, specific conditions existing *in utero*, during development, render each individual unique. Prior to birth the fetal lung serves many important functions, including the production of hormones to regulate fetal growth and development.

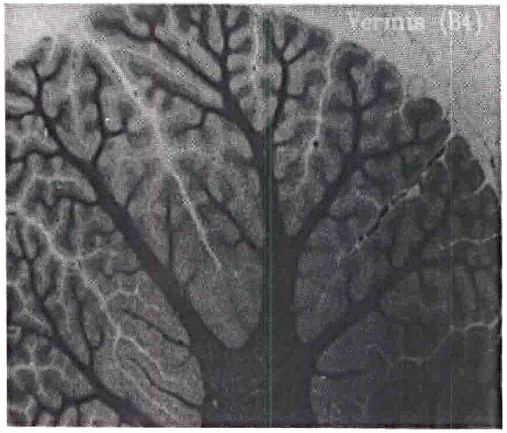
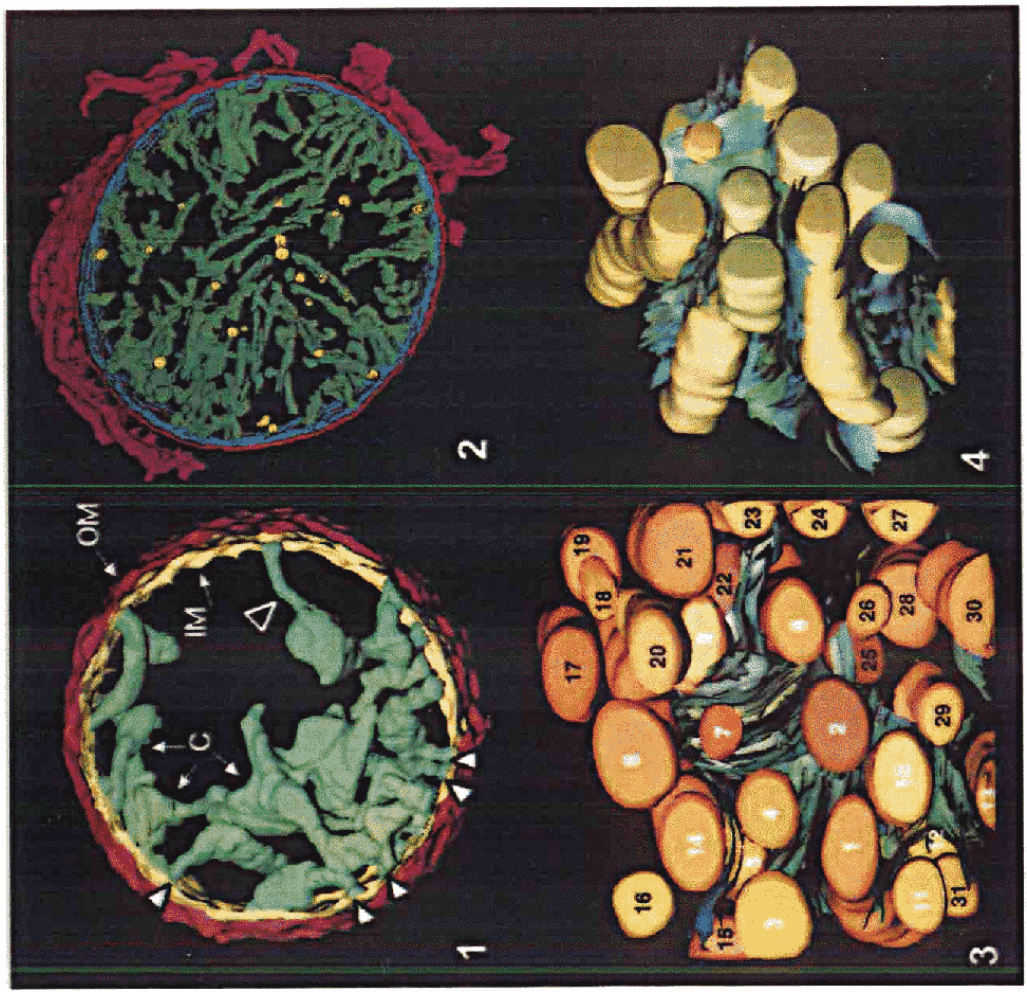


FIGURE 5 A slice through the cerebellum showing the progressive branching structure as the white matter is distributed throughout the cerebellar volume. The geometric complexity of these structures provides for rapid dissemination of information (or resource) via a large surface area in a compact space. This feature is a hallmark of fractal structures which maximize the surface area within a finite volume.



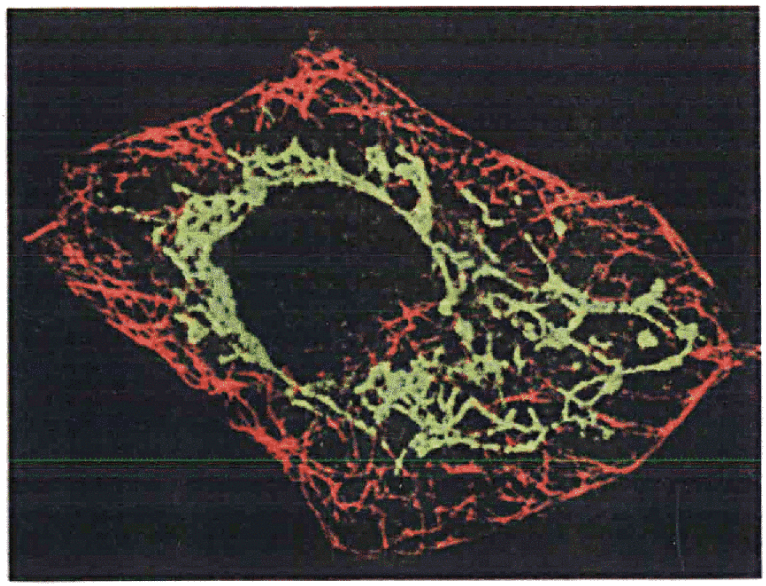
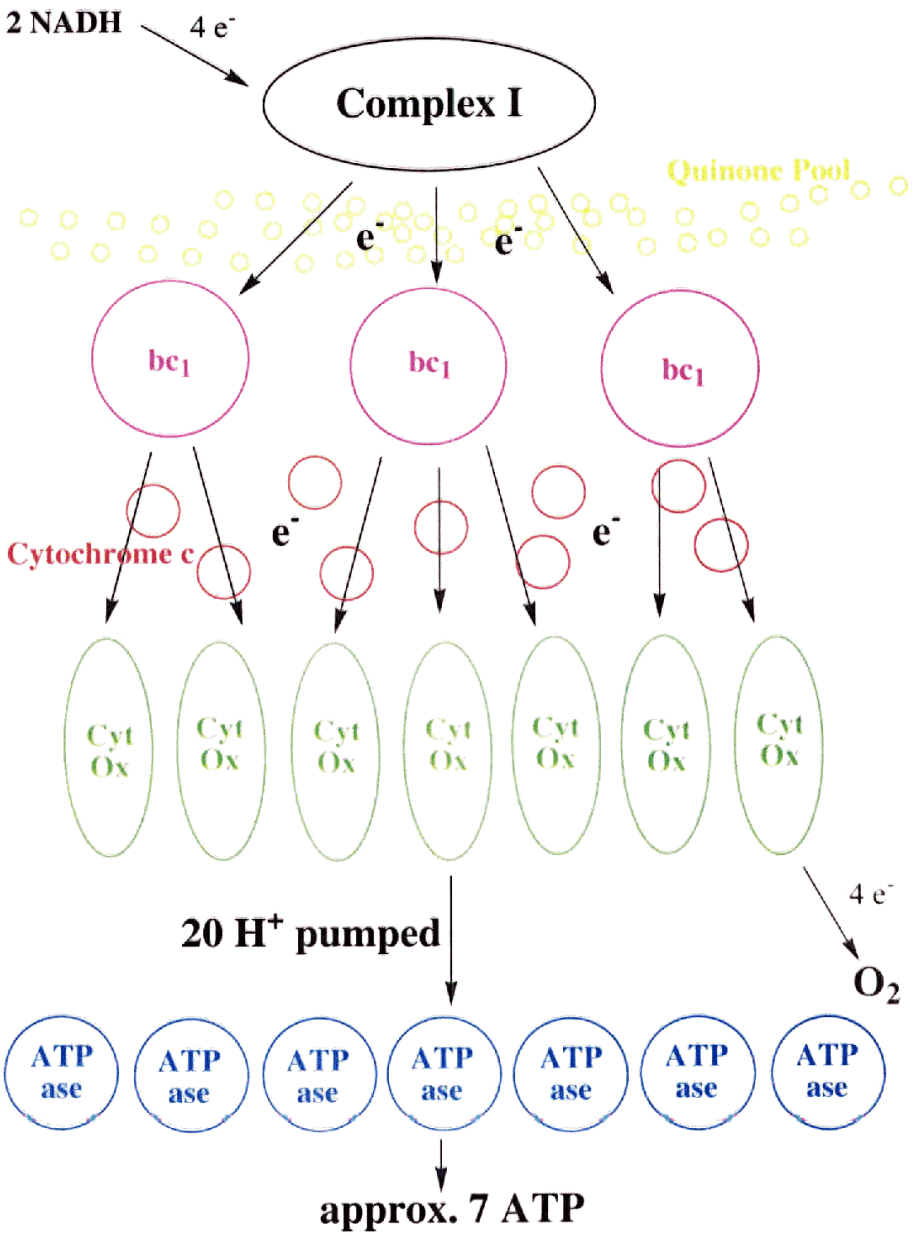
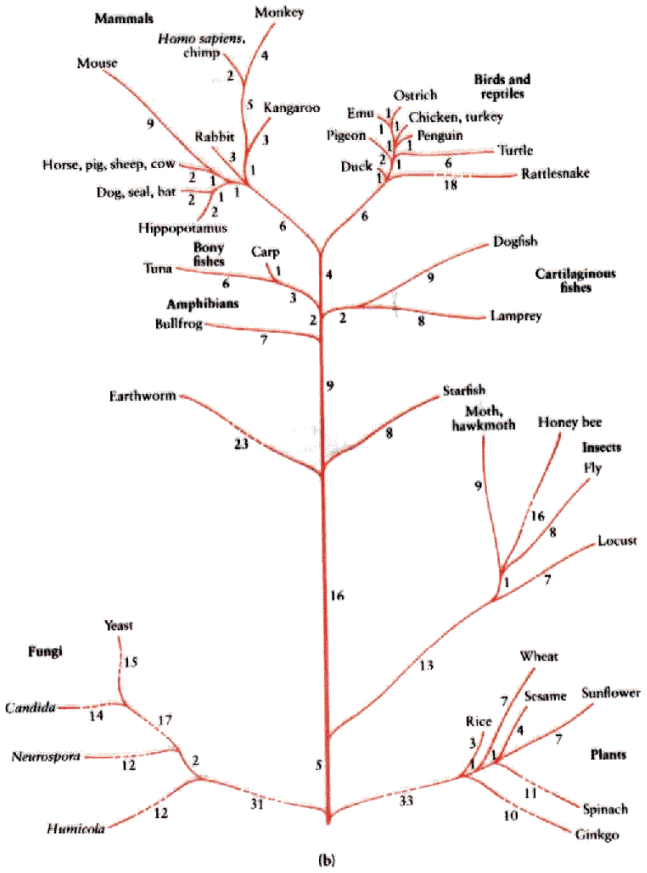


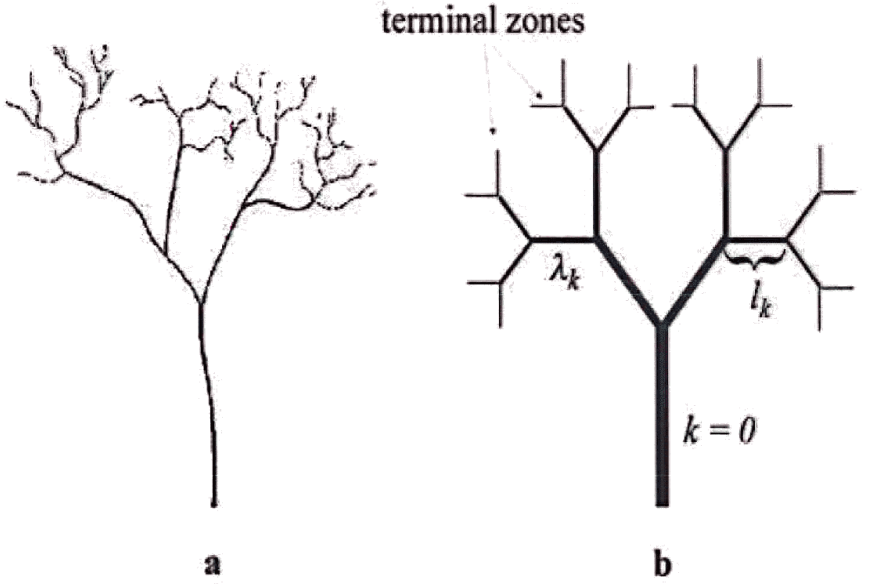
Fig. 1. Mitochondrial network in a mammalian fibroblast. A COS-7 cell labeled to visualize mitochondria (green) and microtubules (red) was analyzed by indirect immunofluorescence confocal microscopy. Mitochondria were labeled with antibodies to the β subunit of the F_1-ATPase and a rhodamine-conjugated secondary antibody. Microtubules were labeled with antibody to tubulin and a fluorescein-conjugated secondary antibody. Pseudocolor was added to the digitized image. Scale: 1 cm = 10 μm.

From M. P. Yaffe, *Science,* **283,** 1493 (1999).


2 NADH
4 e-
Complex I
Quinone Pool
e-
e-
bc1
bc1
bc1
Cytochrome c
e-
e-
Cyt Ox
Cyt Ox
Cyt Ox
Cyt Ox
Cyt Ox
Cyt Ox
Cyt Ox
4 e-
20 H+ pumped
O2
ATP ase
ATP ase
ATP ase
ATP ase
ATP ase
ATP ase
ATP ase
approx. 7 ATP


Mammals
Monkey
Homo sapiens, chimp
Mouse
Kangaroo
Rabbit
Horse, pig, sheep, cow
Dog, seal, bat
Hippopotamus
Birds and reptiles
Ostrich
Emu
Chicken, turkey
Pigeon
Penguin
Turtle
Duck
Rattlesnake
Dogfish
Bony fishes
Tuna
Carp
Cartilaginous fishes
Amphibians
Bullfrog
Lamprey
Earthworm
Starfish
Moth, hawkmoth
Honey bee
Insects
Fly
Locust
Yeast
Fungi
Candida
Neurospora
Humicola
Wheat
Sesame
Sunflower
Rice
Plants
Spinach
Ginkgo
(b)

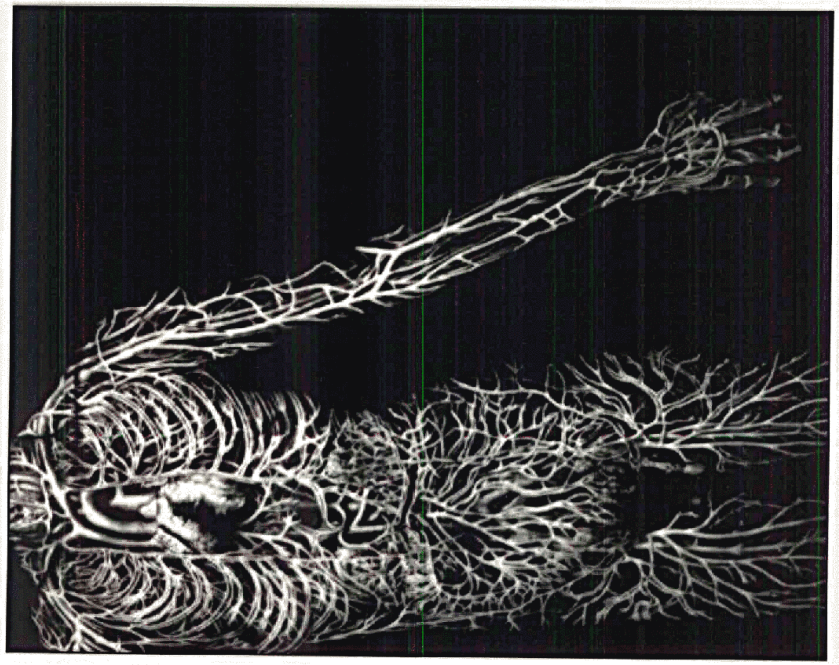
Ant Foraging Trails



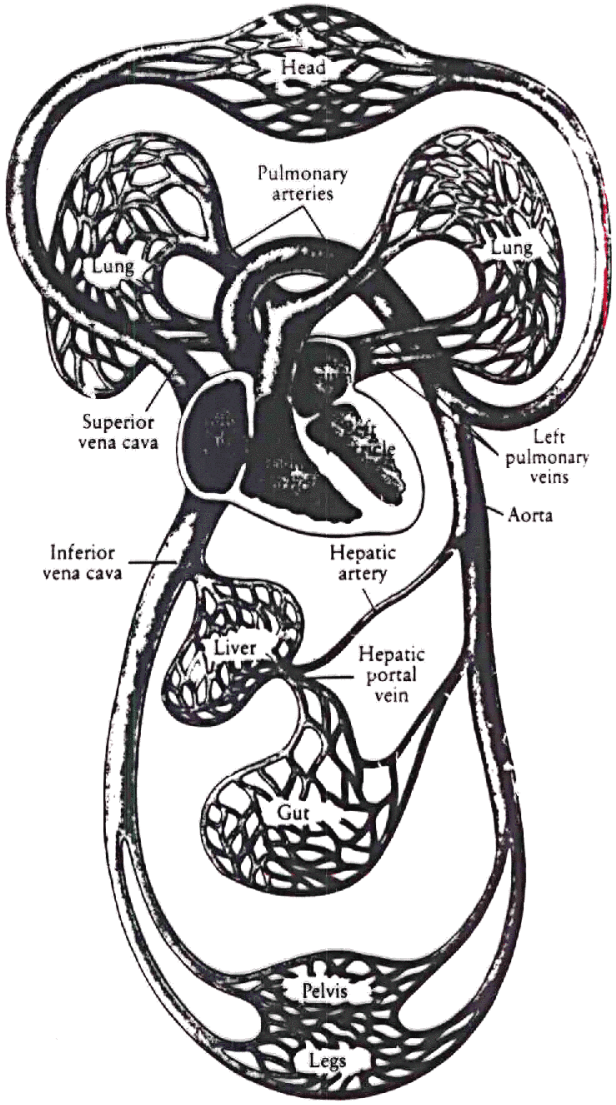
As the colony size (number of ants) increases these trail networks increase in size.

Holldobler and Wilson *The Ants* (1990)

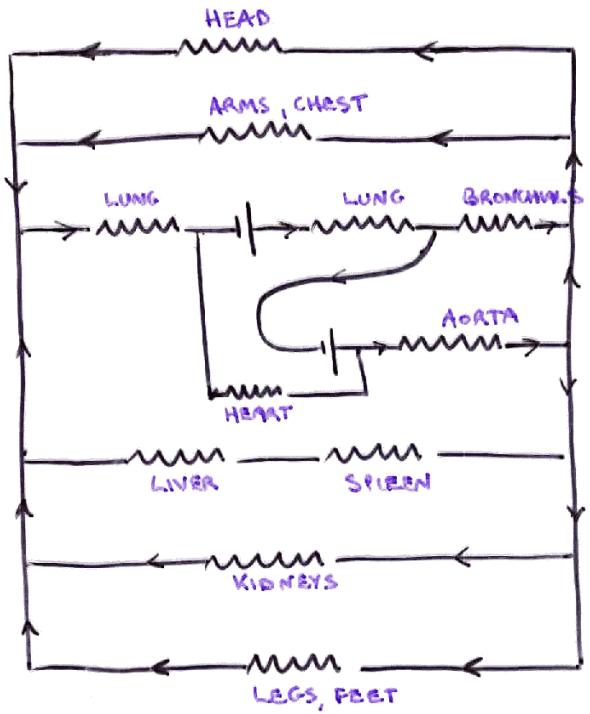
Space-filling,
Hierarchical,
Branching network

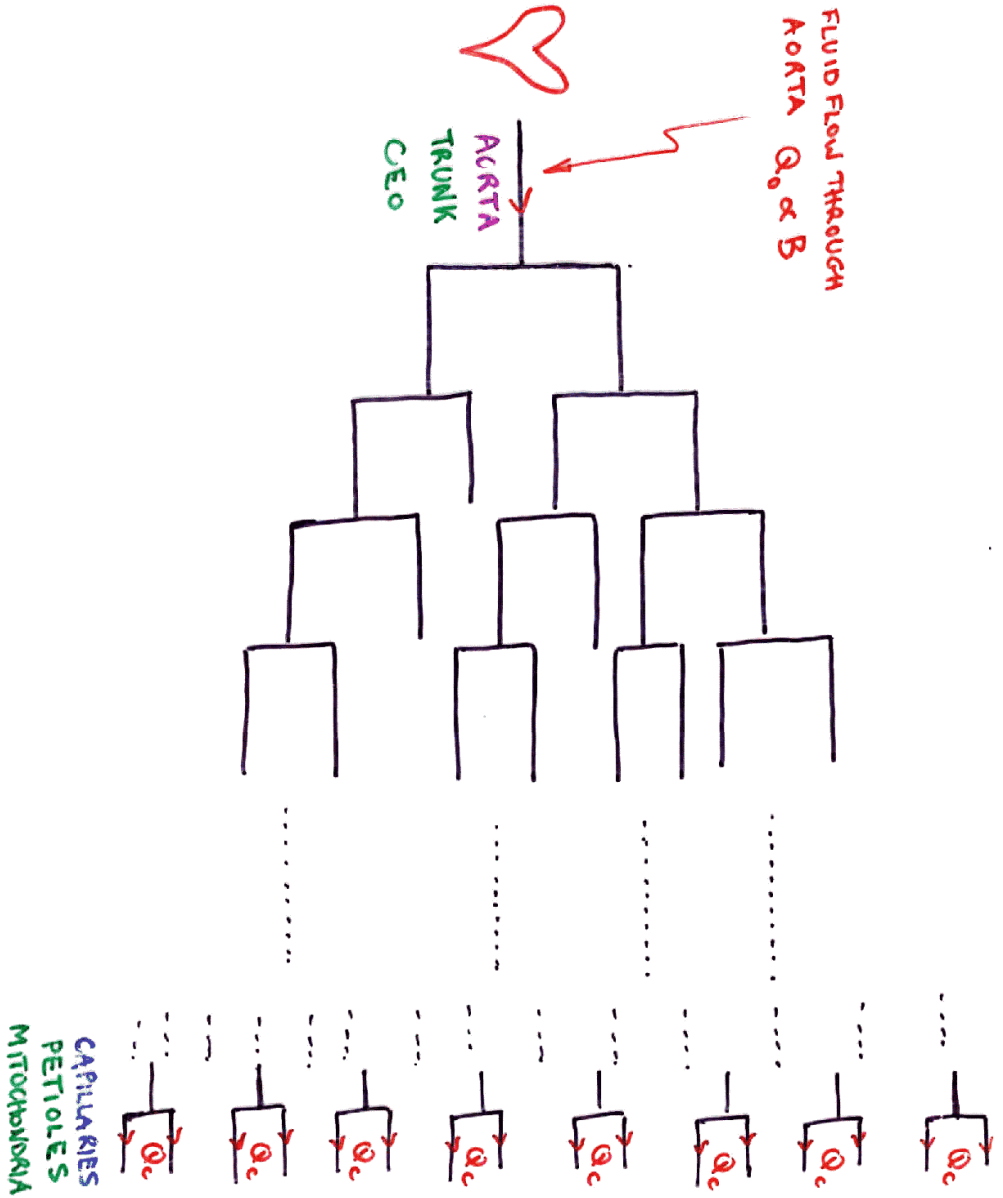


Katherine Du Tiel, 1994



THE VASCULAR CIRCUITRY


HEAD
ARMS, CHEST
LUNG
LUNG
BRONCHIOLES
AORTA
HEART
LIVER
SPLEEN
KIDNEYS
LEGS, FEET


FLUID FLOW THROUGH AORTA Q_0 & B
AORTA
TRUNK
CEO
CAPILLARIES
PETIOLES
MITOCHONDRIA
Q_c

SINCE THE FLUID TRANSPORTS O_2 / NUTRIENTS

$$B \propto \dot{Q}_o$$

CONSERVATION OF FLUID:

$$\dot{Q}_o = N_c \dot{Q}_c = N_c \pi r_c^2 u_c$$

(AORTA) (CAPILLARIES)

$$[\quad = N_k \dot{Q}_k = N_k \pi r_k^2 u_k \quad \text{ANY } k\,]$$

$\Rightarrow$ IF CAPILLARY IS AN INVARIANT UNIT

AND $B \propto M^a$ [a TO BE DETERMINED]

THEN $N_c \propto M^a$

SO IF $a = 3/4$ (TO BE SHOWN)

THEN $N_c \propto M^{3/4}$ NOT $N_c \propto M$

$\Rightarrow$ NUMBER OF CELLS FED BY A SINGLE CAPILLARY INCREASES WITH M

(SINCE NUMBER OF CELLS $\sim M$)

SINCE THE FLUID (BLOOD) TRANSPORTS OXYGEN, NUTRIENTS, ETC FROM THE AORTA TO THE CAPILLARIES

METABOLIC RATE $\propto$ VOLUME FLOW RATE

$$B \propto Q_o$$

BUT THE CONSERVATION OF FLUID (BLOOD)

$\Rightarrow$ $$Q_o = N_c Q_c$$

N_c: TOTAL NUMBER OF CAPILLARIES

Q_c: VOLUME FLOW RATE IN AVERAGE CAPILLARY

CAPILLARY IS AN INVARIANT UNIT

(Q_c IS SAME FOR ALL MAMMALS)

$\Rightarrow$ NUMBER OF CAPILLARIES (N_c) MUST SCALE IN SAME WAY AS THE METABOLIC RATE ($B \propto Q_o$)

SO, IF $B \sim M^{3/4}$ THEN

$N_c \sim M^{3/4}$ (NOT $N_c \sim M$)

TOTAL NUMBER OF CELLS

$N_{cell} \sim M$ (LINEAR)

TOTAL NUMBER OF CAPILLARIES

$N_c \sim M^{3/4}$

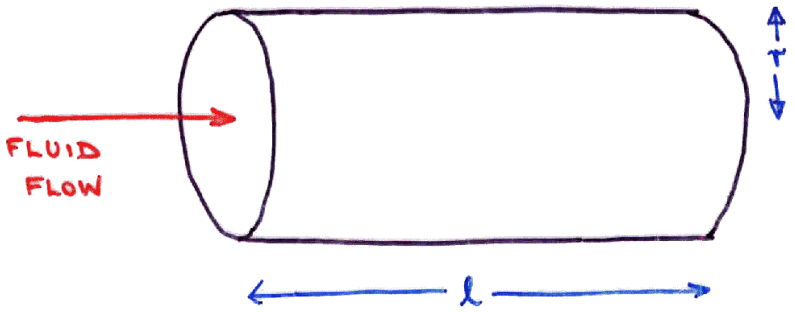
MISMATCH !

$\Rightarrow$ NUMBER OF CELLS FED BY A SINGLE CAPILLARY INCREASES AS $M^{1/4}$

(ANOTHER MANIFESTATION THAT EFFICIENCY INCREASES WITH SIZE)

IMPORTANT IMPLICATIONS FOR GROWTH AND DEATH !

SCALING OF LENGTHS AND RADII



HOW DO RADII AND LENGTHS OF TUBES CHANGE (SCALE) THROUGH THE NETWORK ?

1) SPACE-FILLING

GENERAL PROPERTY OF ALL NETWORKS REGARDLESS OF STRUCTURE

NETWORK SERVICES ALL "BIOLOGICAL" ("FUNCTIONAL") SPACE DEFINED BY THE ORGANISM

[DETERMINES SCALING OF LENGTHS]

$$N_k \, \ell_k^d \approx N_{k+1} \, \ell_{k+1}^d$$

"VOLUME PRESERVING"

NUMBER OF BRANCHES OF SIZE (ORDER) ℓ_k

d-DIMENSIONAL VOLUME OF SPACE "FILLED" OR "SERVICED" BY BRANCH OF SIZE ℓ_k (ORDER k)

$$\Rightarrow \gamma_k \equiv \frac{\ell_{k+1}}{\ell_k} = \left(\frac{N_k}{N_{k+1}}\right)^{1/d} = \frac{1}{n^{1/d}}$$

BRANCHING RATIO (n)

3-d: $\boxed{\gamma = \frac{1}{n^{1/3}}}$ INDY. OF k

SPACE-FILLING GIVES

$$\frac{\ell_{k+1}}{\ell_k} = \frac{1}{2^{1/3}} = \frac{1}{\sqrt[3]{2}}$$

3 DIMENSIONS

IF BRANCHING IS DICHOTOMOUS

[GENERALLY, $\frac{\ell_{k+1}}{\ell_k} = \frac{1}{n^{1/d}} = \frac{1}{\sqrt[d]{n}}$]

② STRUCTURE AND DYNAMICS

FOR PLANTS/TREES, EACH BRANCH IS A TIGHT BUNDLE OF TUBES RUNNING FROM ROOT TO LEAF ⇒ BRANCHING IS

"AREA-PRESERVING"

THE CROSS-SECTIONAL AREA OF A PARENT BRANCH = THE SUM OF THE CROSS-SECTIONAL AREAS OF ITS DAUGHTERS

EXTEND SPACE-FILLING CONCEPT TO NETWORK:

AT ALL SCALES NEED TO SERVICE ALL LOCAL VOLUMES OF ORGANISM'S TISSUE

$$\Rightarrow \quad \frac{l_{k+1}}{l_k} = \frac{1}{2^{1/3}} \qquad \frac{1}{\sqrt[3]{2}}$$

RATIO OF BRANCH LENGTHS IN THE HIERARCHY

k DENOTES LEVEL IN THE HIERARCHY

[GENERALISATION:

$$\frac{l_{k+1}}{l_k} = \frac{1}{n^{1/d}}$$

SO THE "2" REFLECTS BIFURCATION

AND "1/3" REFLECTS DIMENSIONALITY OF SPACE]

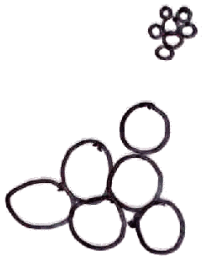
SUBDIVIDE SPACE INTO SMALL VOLUMES OF SIZE ϵ^3

e.g. SPHERES OF RADIUS ϵ

IF $\epsilon \propto$ SIZE OF BRANCH AT LEVEL k, l_k

THEN VOLUME "SERVICED" BY NETWORK IS

$$N_k \, l_k^3$$



(2) "AREA-PRESERVING" BRANCHING

DYNAMICS (FOR MANY SYSTEMS) (TO BE PROVEN)

$$\Rightarrow \quad \pi r_k^2 = n \pi r_{k+1}^2$$

- r_k: X-SECTIONAL AREA OF PARENT BRANCH
- n: NUMBER OF DAUGHTERS (BRANCHING RATIO)
- r_{k+1}: X-SECTIONAL AREA OF EACH DAUGHTER

[KNOWN TO LEONARDO !!]

$$\Rightarrow \beta_k \equiv \frac{r_{k+1}}{r_k} = \frac{1}{n^{1/2}} = \frac{1}{\sqrt{2}}$$

BIFURCATIONS

$$\boxed{\beta = \frac{1}{n^{1/2}}}$$

IND? OF k

$\Rightarrow$ i) MAXIMUM SIZE FOR MAMMALS

ii) POSSIBILITY OF ECOSYSTEM

STRUCTURE AND DYNAMICS

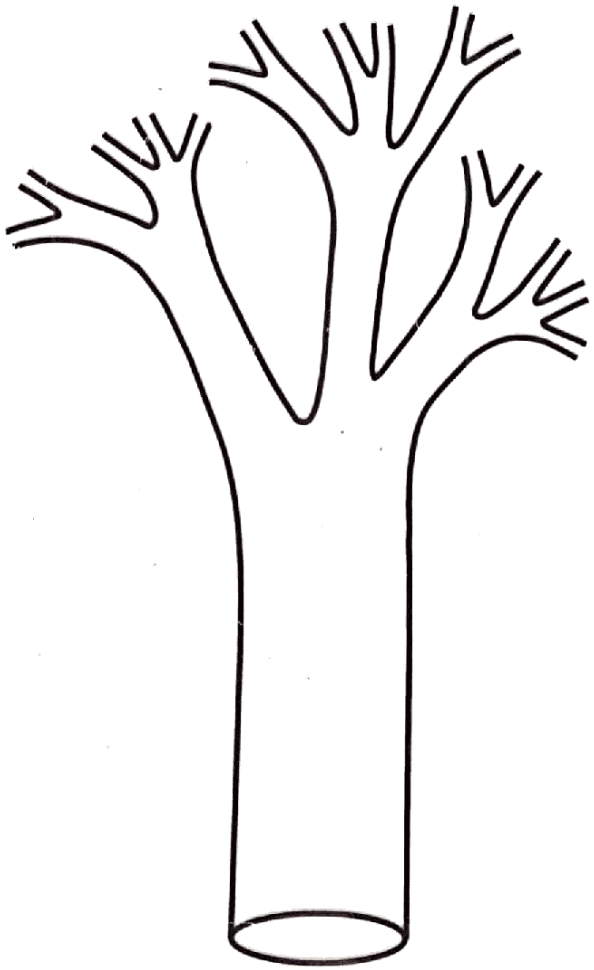
OPTIMAL DESIGN (NATURAL SELECTION)

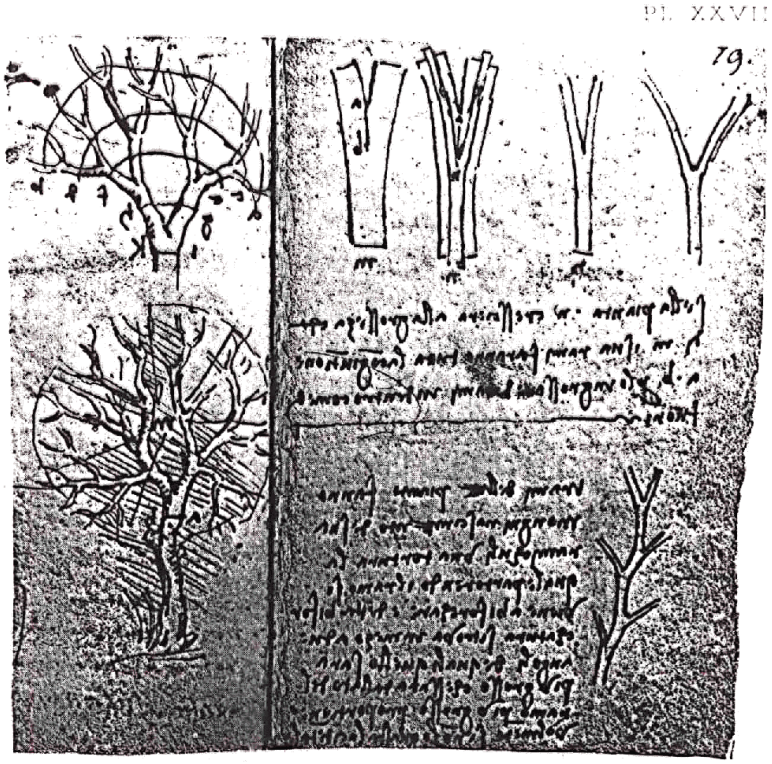
$\Rightarrow$ "AREA-PRESERVING BRANCHING"

RATIO OF TUBE RADII IN THE HIERARCHY

$$\frac{r_{k+1}}{r_k} = \frac{1}{2^{1/2}} \qquad \frac{1}{\sqrt[3]{2}}$$

[MORE GENERALLY $\frac{r_{k+1}}{r_k} = \frac{1}{n^{1/2}} = \frac{1}{\sqrt{n}}$]




PL. XXVII
79.

DERIVATION OF 3/4 EXPONENT

HAVE SCALING WITHIN ORGANISM

- NEED TO RELATE TO MASS M

ASSUME (TO BE PROVEN) THAT

TOTAL VOLUME OF FLUID IN NETWORK, $V_b \propto M$

$$V_b = \sum_{k=0}^{N} N_k V_k$$

(N_k: TOTAL NUMBER OF BRANCHES AT LEVEL k; V_k: VOLUME OF TUBE)

$$= \sum_{k=0}^{N} \pi r_k^2 l_k n^k$$

$$\propto (\gamma \beta^2)^{-N} V_c$$

(V_c: VOLUME OF CAPILLARY)

RECALL: IF $B \propto M^a \Rightarrow N_c = n^N \propto M^a$ (FLUID CONSERVATION)

(M^a: DEFINITION OF a; N_c: TOTAL NUMER OF CAPILLARIES)

IF $V_b \propto M$ AND $V_c \propto M^0$:

$$\Rightarrow a = \frac{\log n}{\log (\gamma \beta^2)}$$

WITH $\gamma = n^{-1/3}$ (SPACE-FILLING)

$\beta = n^{-1/2}$ (AREA-PRESERVING)

$$\Rightarrow a = \frac{3}{4}$$ (INDEPENDENT OF n)

MORE GENERALLY: IN d-DIMENSIONS

$$\gamma = n^{-1/d}, \quad \beta = n^{-1/2}$$

$$\Rightarrow a = \frac{1}{\frac{1}{d} + 2 \times \frac{1}{2}}$$

($\frac{1}{d}$: SPACE-FILLING (γ); $2 \times \frac{1}{2}$: X-SECTIONAL AREA OF TUBE; $\frac{1}{2}$: AREA-PRESERVING (β))

$$= \frac{d}{d+1}$$

($\frac{1}{\frac{1}{d}+1}$)

"EVERYTHING" FOLLOWS FROM THE 4 BASIC PRINCIPLES

I. HIERARCHICAL "FRACTAL-LIKE" BRANCHING NETWORKS

II. SPACE-FILLING

III. INVARIANT TERMINAL UNITS

IV. ENERGY DISSIPATED IS MINIMISED

II $\Rightarrow$ i) SPACE-FILLING $\frac{l_{k+1}}{l_k} = \frac{1}{2^{1/3}}$

III $\Rightarrow$ ii) INV. TERMINAL UNITS

IV $\Rightarrow$ iii) AREA-PRESERVING BRANCHING $\frac{r_{k+1}}{r_k} = \frac{1}{2^{1/2}}$

IV $\Rightarrow$ iv) VOLUME OF NETWORK (BLOOD) ~ VOLUME OF WHOLE BODY ~ M

$\Rightarrow B \propto M^{3/4}$ (AND MUCH MORE)

IN d DIMENSIONS

$$B \propto M^{\frac{d}{d+1}}$$

WE LIVE IN 3 SPATIAL DIMENSIONS SO $B \propto M^{3/4}$

$\Rightarrow$ "3" REPRESENTS DIMENSIONALITY OF SPACE

"4" INCREASE IN DIMENSIONALITY DUE TO FRACTAL-LIKE SPACE FILLING

LIFE HAS TAKEN ADVANTAGE OF THE POSSIBILITY OF USING SPACE-FILLING FRACTAL-LIKE SURFACES (WHERE ENERGY AND RESOURCES ARE EXCHANGED) TO MAXIMISE ENERGY TRANSFER FROM THE ENVIRONMENT

NON-FRACTAL : $M^{2/3}$ ← AREA; ← DIMENSIONALITY OF SPACE (VOLUME)

BIOLOGICAL (FRACTAL) $M^{3/4}$

BY ANALOGY : LIFE EFFECTIVELY OPERATES IN FOUR SPATIAL DIMENSIONS

[FIVE IF TIME IS INCLUDED]

F FURTHER SCALING LAWS

1) $r_0 = \beta^{-N} r_c$

$r_0 = N_c^{1/3} r_c \propto M^{3/8}$

- r_0: RADIUS OF AORTA (TRUNK)
- $N_c^{1/3}$: NUMBER OF CAPILLARIES (PETIOLES)
- r_c: RADIUS OF CAPILLARY (PETIOLE)

$$l_0 \propto M^{1/4}$$
$$r_0 \propto M^{3/8}$$

β AND γ PLAY DUAL SCALING ROLE :

i) SCALING WITHIN A SINGLE ORGANISM

ii) SCALING BETWEEN ORGANISMS

e.g. $\frac{r_0}{r_c} \approx 9 \times 10^3$ IN HUMANS

6) HYDRODYNAMIC RESISTANCE OF THE NETWORK

$$\sim \frac{1}{M^{3/4}}$$

TOTAL RESISTANCE DECREASES WITH SIZE !!

SMALL MAY BE BEAUTIFUL BUT LARGE IS MORE EFFICIENT !!

7) BLOOD PRESSURE $\sim M^0$

AORTA BLOOD VELOCITY $\sim M^0$

} INVARIANT !

RADIUS OF A WHALE'S AORTA $\sim$ 30 cm

RADIUS OF A SHREW'S AORTA $\sim \frac{1}{10}$ mm

YET THEY HAVE THE SAME BLOOD PRESSURE AND VELOCITY OF BLOOD LEAVING THEIR HEARTS (AS YOU DO) !

FIND $Z_{TOT} \propto \frac{1}{N_c} \propto \frac{1}{M^a} = \frac{1}{M^{3/4}}$

IE. TOTAL RESISTANCE DECREASES WITH SIZE OF ORGANISM

SMALL MAY BE BEAUTIFUL BUT LARGE IS MORE EFFICIENT !!

REMARKABLE CONSEQUENCES :

i) BLOOD PRESSURE

$$\Delta p = \dot{Q}_o Z_{TOT} \propto M^0$$

ii) BLOOD VELOCITY

$$u_o \propto M^0$$

} BOTH INVARIANT!

(8) $\frac{\text{VELOCITY OF BLOOD IN AORTA}}{\text{VELOCITY OF BLOOD IN CAPILLARY}} \approx 250$

BUT IN A PLANT (OR TREE) VELOCITY UNCHANGED FROM TRUNK TO LEAF

⇓

WHERE DOES AREA-PRESERVING COME FROM IN MAMMALS?

WHY DOES BLOOD SLOW DOWN? NECESSARY FOR EFFICIENT TRANSFER OF NUTRIENTS TO CELLS.

(9) UPPER PART OF SYSTEM (AORTA AND ARTERIES)

AREA-PRESERVING : NO ENERGY LOSS

("IMPEDANCE MATCHING" – AS IN ELECTRICAL TRANSMISSION ACROSS COUNTRY – NO REFLECTED WAVE AT BRANCH POINTS)

LOWER PART OF SYSTEM (ARTERIOLES, CAPILLARIES)

ENERGY LOSS (DUE TO VISCOSITY): BLOOD SLOWS DOWN, WAVE IS DISSIPATED; AREA INCREASING

TURNOVER POINT IS SAME FOR ALL MAMMALS!

ONLY DISTINGUISHED BY NUMBER IN UPPER PART WHERE THERE IS AREA-PRESERVING

[e.g. SHREW ~1; HUMANS ~5, WHALE ~15]

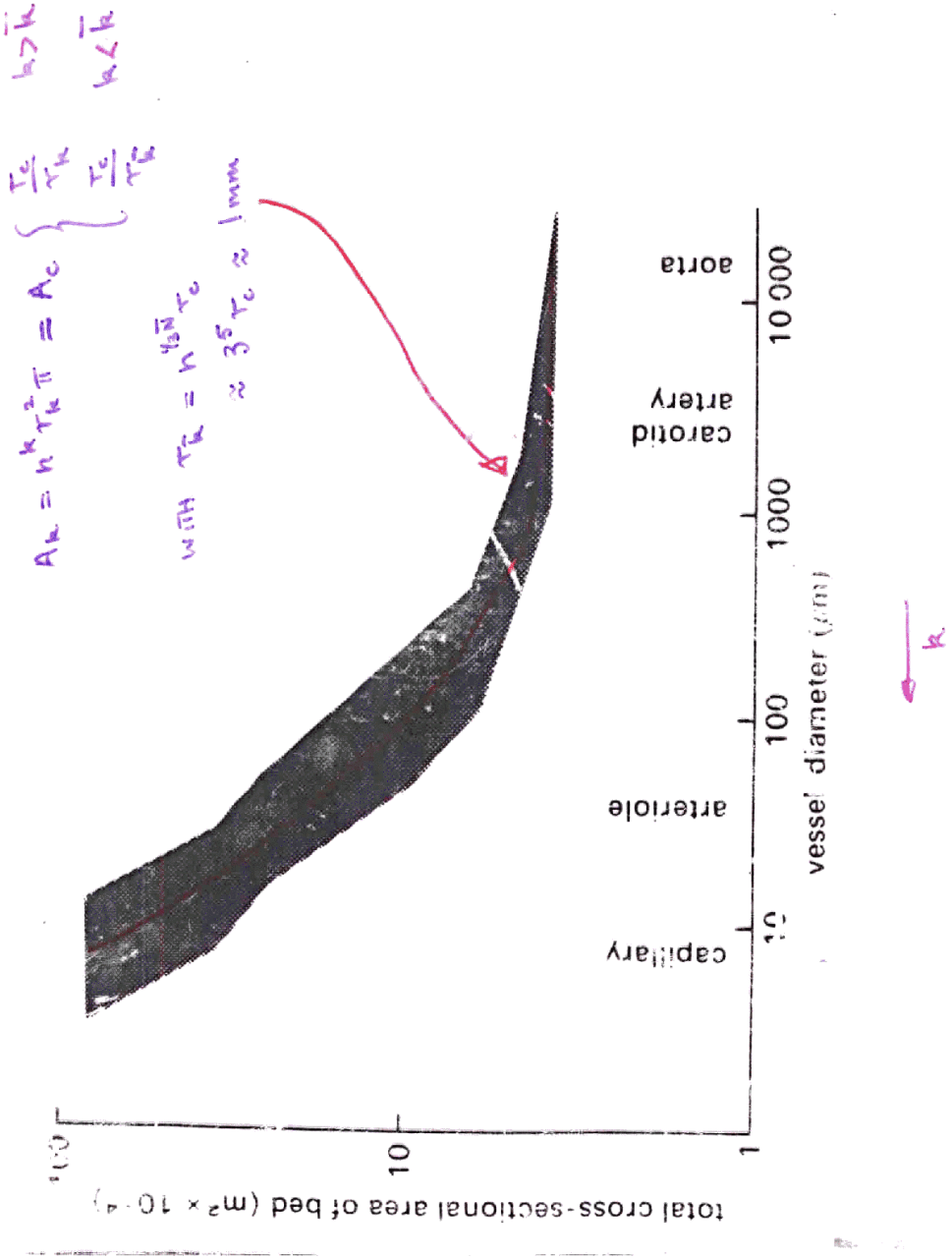
TABLES

TABLE I. Values of allometric exponents for variables of the mammalian circulatory system predicted by the model compared with empirical observations. The radius, length and velocity of blood in the capillary are all assumed to be independent of M. References not cited above can be found in refs. 2 and 3.

VARIABLE	SCALING EXPONENT		REFERENCE
CIRCULATORY SYSTEM	PREDICTED	OBSERVED	
Radius of Aorta, r_0	$\frac{3}{8} = 0.375$	0.36	Holt et al. 1981
Pressure in Aorta, Δp_0	$0 = 0.00$	0.032	Gunther & de la Barra, 1966
Velocity of Blood in Aorta, u_0	$0 = 0.00$	0.07	Milnor, 1979
Blood Volume, V_b	$1 = 1.00$	1.00	Prothero, 1980
Circulation Time	$\frac{1}{4} = 0.25$	0.25	Schmidt-Nielsen, 1984
Circulation Distance, l	$\frac{1}{4} = 0.25$	Not Available	–
Cardiac Stroke Volume	$1 = 1.00$	1.03	Gunther, 1975
Cardiac Frequency, ω	$-\frac{1}{4} = -0.25$	−0.25	Stahl, 1981
Cardiac Output, $\dot{E}$	$\frac{3}{4} = 0.75$	0.74	Gunther, 1975
Number of Capillaries, N_c	$\frac{3}{4} = 0.75$	Not Available	–
Supply Radius of Cells	$\frac{1}{12} = 0.083$	Not Available	
Radius of Krogh Cylinder	$\frac{1}{8} = 0.125$	Not Available	–
Density of Capillaries	$-\frac{1}{12} = -0.083$	−0.095	Hoppeler et al., 1981
Oxygen Affinity of Blood, P_{50}	$-\frac{1}{12} = -0.083$	−0.089	Dhindsa et al., 1971
Total Peripheral Resistance, Z	$-\frac{3}{4} = -0.75$	0.76	Gunther, 1975
Womersley Number, α	$\frac{1}{4} = 0.25$	0.25	–
Metabolic Rate, B	$\frac{3}{4} = 0.75$	0.75	Stahl, 1967

TABLE II. Values of allometric exponents for variables of the mammalian respiratory system predicted by the model compared with empirical observations. References not cited above can be found in refs. 2 and 3.

VARIABLE	SCALING EXPONENT		REFERENCE
RESPIRATORY SYSTEM	PREDICTED	OBSERVED	
Lung Volume	$1 = 1.00$	1.05	Weibel, 1973
Respiratory Frequency	$-\frac{1}{4} = -0.25$	−0.26	Stahl, 1967
Volume Flow to Lung	$\frac{3}{4} = 0.75$	0.80	Stahl, 1967
Interpleural Pressure	$0 = 0.00$	0.004	Gunther & de la Barra, 1966
Diameter of Trachea	$\frac{3}{8} = 0.375$	0.39	Tenney & Bartlett, 1967 and pers. comm. in Calder, 1984
Air Velocity in Trachea	$0 = 0.00$	0.02	Calder (calculated), 1984
Tidal Volume	$1 = 1.00$	1.041	Maina & Settle, 1982
Power Dissipated	$\frac{3}{4} = 0.75$	0.78	Stahl, 1967
Number of Alveoli, N_A	$\frac{3}{4} = 0.75$	Not Available	–
Volume of Alveolus, V_A	$\frac{1}{4} = 0.25$	Not Available	–
Radius of Alveolus, r_A	$\frac{1}{12} = 0.083$	0.13	Tenney & Remmers, 1963
Surface Area of Alveolus, A_A	$\frac{1}{6} = 0.083$	Not Available	
Surface Area of Lung, A_L	$\frac{11}{12} = 0.92$	0.95	Gehr et al., 1981
Oxygen Diffusing Capacity	$1 = 1.00$	0.99	Gehr et al., 1981
Total Airway Resistance	$-\frac{3}{4} = -0.75$	0.70	Stahl, 1967
Oxygen Consumption Rate	$\frac{3}{4} = 0.75$	0.76	Stahl, 1967



MAMMALS TO MOLECULES

RESPIRATORY COMPLEX – MITOCHONDRIA – CELLS – ORGANISMS – ECOSYSTEMS

STRINGS MEMBRANES – QUARKS, GLUONS ELECTRONS – HADRONS (PROTONS.....) – NUCLEI – ATOMS MOLECULES

..... ← MATTER

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

BUT TOTAL NUMBER OF CELLS IN ORGANISM $\propto M$

$\therefore$ METABOLIC RATE OF AVERAGE SINGLE CELL (IN VIVO)

$$B_c \propto \frac{B}{M} \propto \frac{M^{3/4}}{M} \propto \frac{1}{M^{1/4}}$$

DECREASES WITH INCREASING BODY SIZE

(ANOTHER MANIFESTATION OF EFFICIENCY INCREASING WITH M)

THIS IS DRIVEN BY HEGEMONY OF THE NETWORK

-STS : REMOVE NETWORK SO CELLS BECOME FREE $\Rightarrow$ B_c (IN VITRO) INDEPENDENT OF ORIGIN (I.E. WHAT MAMMAL THEY ORIGINATED IN).

CROSS-OVER BETWEEN

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

AND $B \propto M$

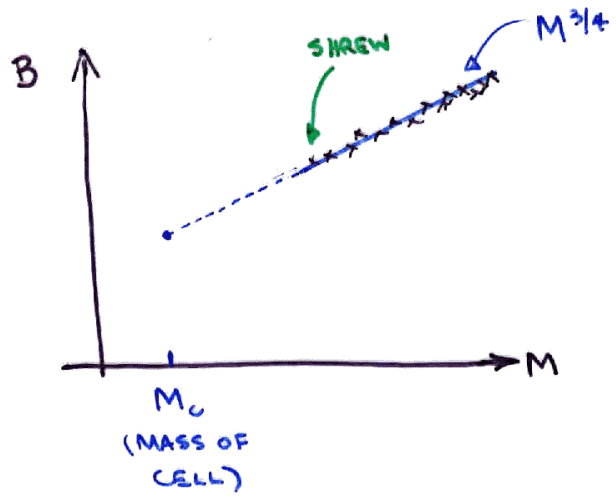
(WHICH OCCURS AT $M \approx \mu$)

OCCURS WHEN THE AORTA IS SO SMALL IT CANNOT SUPPORT A PULSATILE WAVE. NETWORK BECOMES DOMINATED BY VISCOSITY (FLUID FRICTION) – LOTS OF ENERGY IS DISSIPATED AND EFFICIENCY DROPS DRAMATICALLY

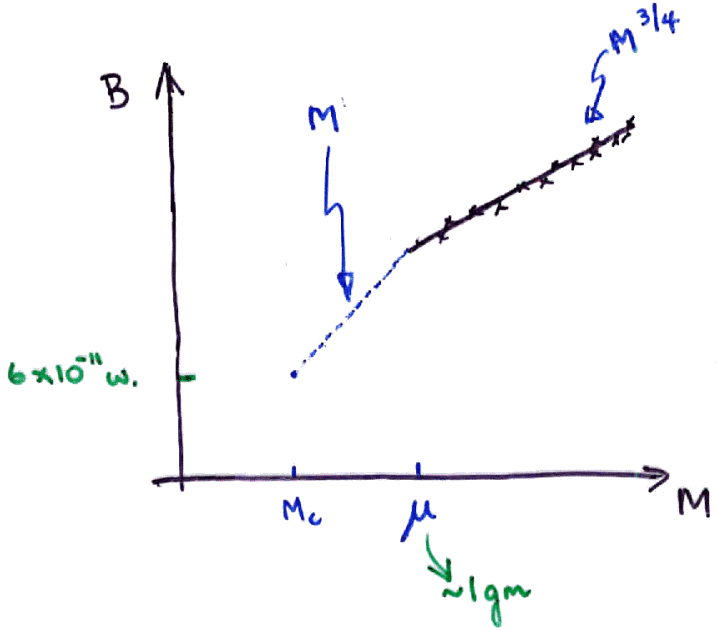
$\Rightarrow$ CAN CALCULATE MASS OF THE SMALLEST MAMMAL : $M_{SMALLEST} \approx \mu \approx 1$ gm.

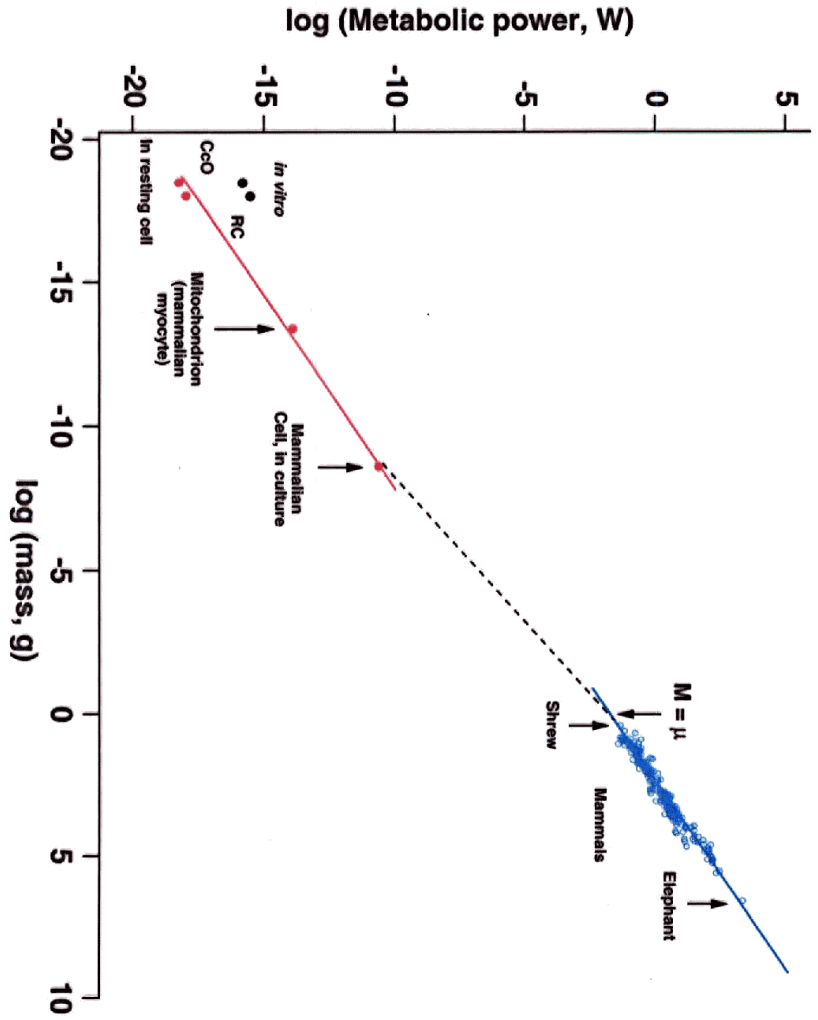
$\Rightarrow$ CELLS ARE WORKING AT THEIR MAXIMUM POSSIBLE RATE IN SHREWS !

[NO WONDER THEY DON'T LIVE VERY LONG !]



NAIVE EXTRAPOLATION OF $M^{3/4}$ WRONG!





THIS DECREASE OF B_c WITH SIZE IS DRIVEN

BY THE HEGEMONY OF THE NETWORK

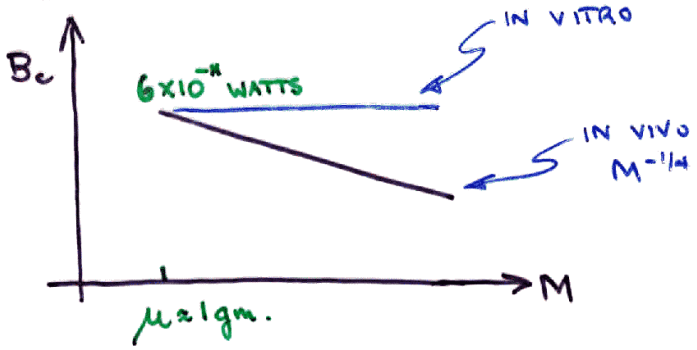
(CONTROLS FUNDAMENTAL BIOCHEMICAL RATES)

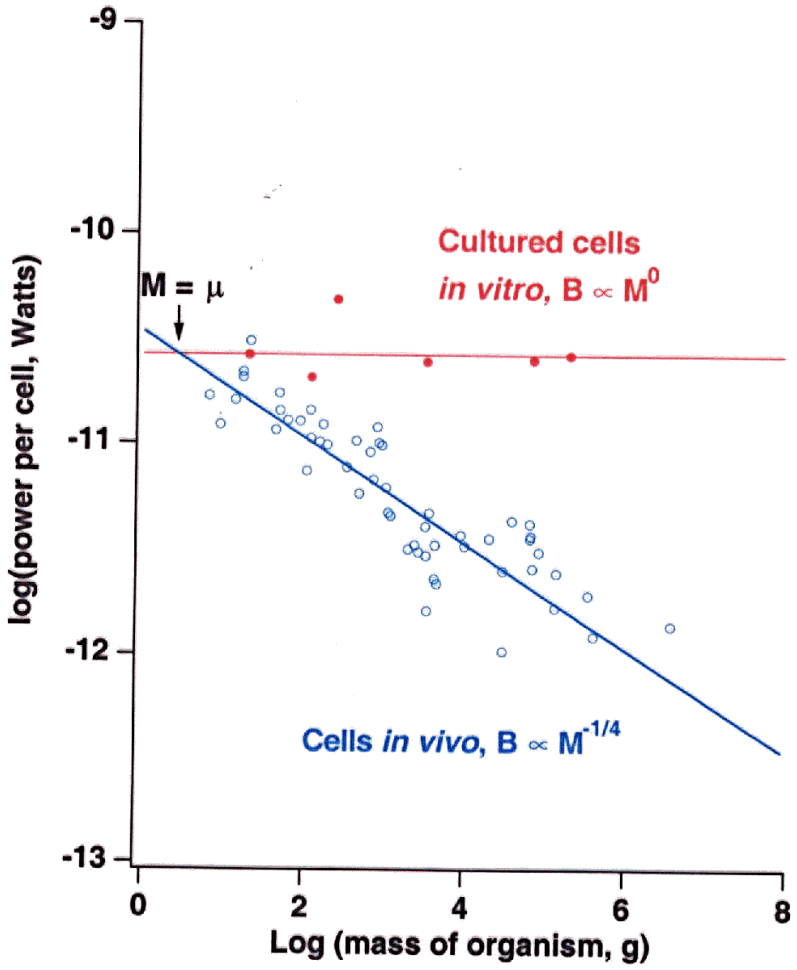
⇒ IF THE NETWORK WERE REMOVED SO CELLS

BECOME FREE (IN VITRO) B_c SHOULD BECOME

INDEPENDENT OF WHAT MAMMAL THEY ORIGINATED

IN: PREDICT





(11)

vi) SUMMARY

ENTIRE PLOT OF MET. RATE vs. MASS COVERING 27 ORDERS OF MAGNITUDE FROM MOLECULES OF THE RESPIRATORY COMPLEX TO MAMMALS CAN BE UNDERSTOOD IN TERMS OF 3 PARAMETERS :

B_o, b, AND μ

$b \approx 0.75$ AND $\mu \approx 1$ gm ARE DETERMINED BY THE MODEL

NOTE POWER GENERATED BY UNCOUPLED RC

$\sim$ 300 X COUPLED RC

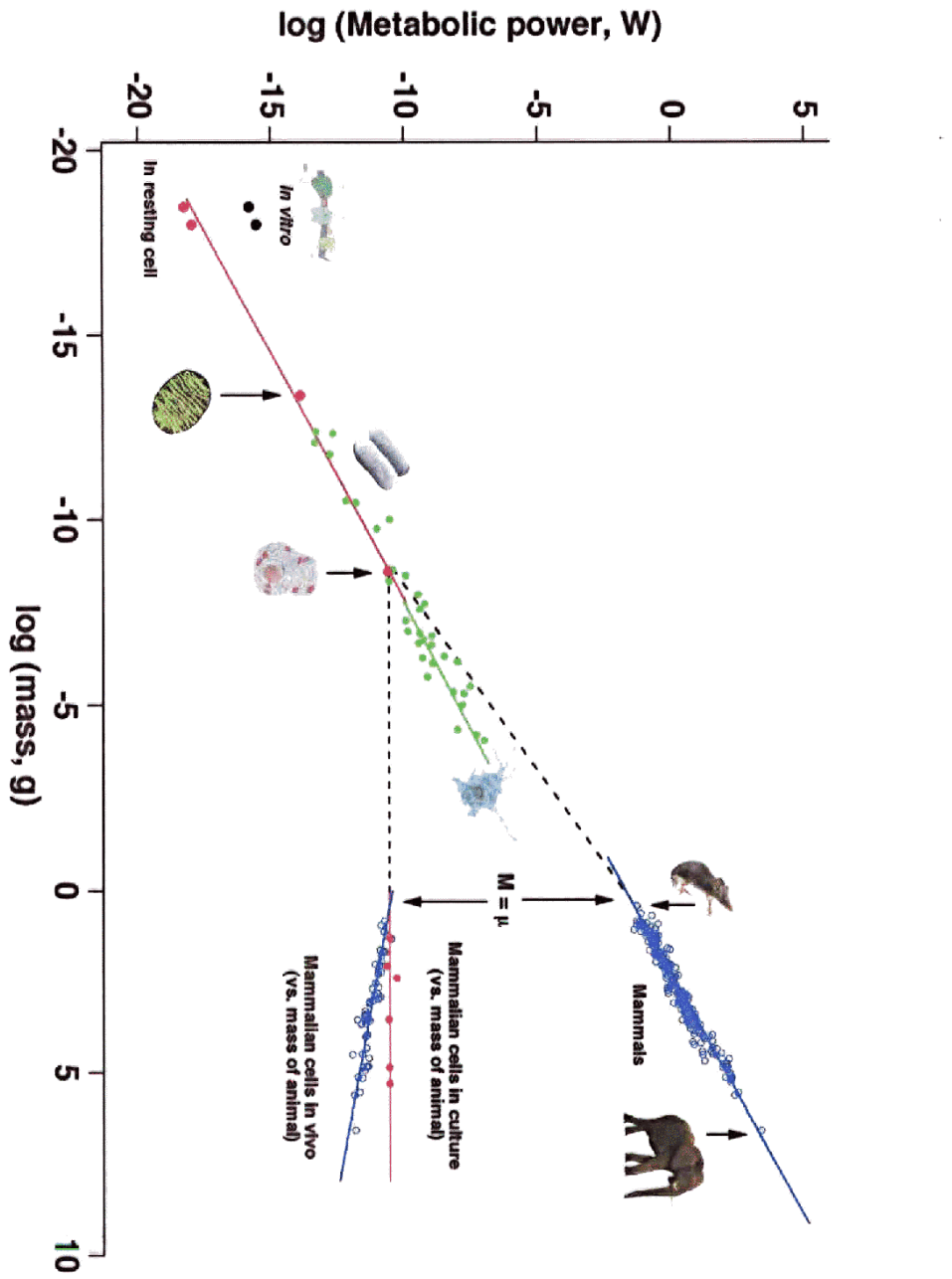
$\Rightarrow$ MAX. POSSIBLE METABOLIC OUTPUT FOR AEROBIC METABOLISM $\sim$ 300X BASAL RATE

TYPICALLY ACTUAL FACTOR IS $\sim$ 20-30 SINCE ONLY A PORTION OF RC's SUPPLY MUSCLE TISSUE

[HOWEVER: ROWERS BURN 7000 KCAL / 20 MINS

$\approx 7000 \times 3 \times 24$ KCAL/DAY

BASAL RATE $\approx$ 3500 KCAL/DAY $\Rightarrow$ INCREASE BY A FACTOR



GROWTH

INCOMING ENERGY (TOTAL METABOLIC RATE)

= NUMBER OF CELLS IN BODY × METABOLIC RATE OF EACH CELL

(MAINTENANCE)

+

ENERGY TO CREATE A CELL × RATE OF INCREASE OF NUMBER OF CELLS

(GROWTH)

$$B = N_c B_c + E_c \dot{N}_c$$

$$\Rightarrow \text{GROWTH RATE} \propto B - N_c B_c$$

$M^{-1/4}$ (CONSTANT THROUGHOUT GROWTH)

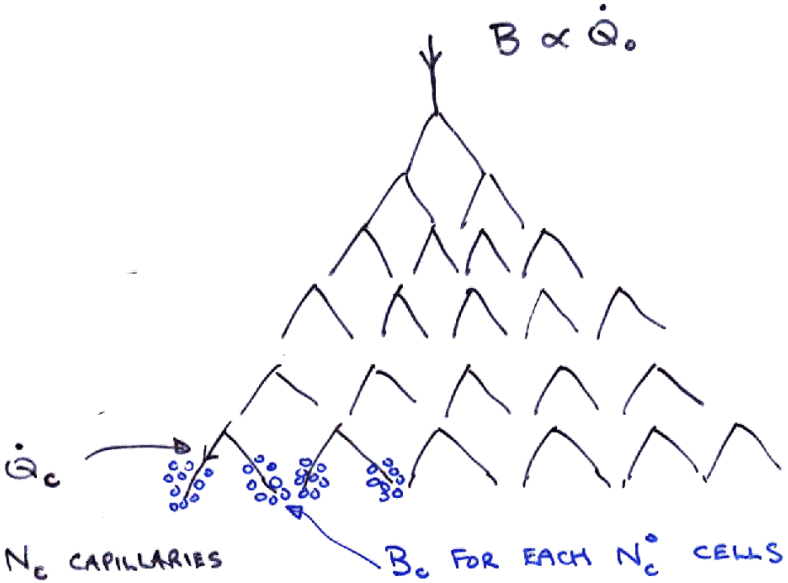
$M^{3/4}$ (NUMBER OF CAPILLARIES)

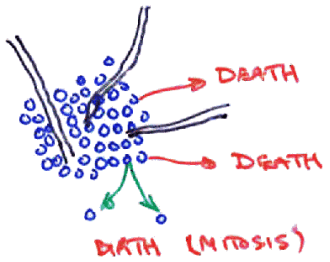
M (NUMBER OF CELLS)

STOP GROWING AND REACH AN ASYMPTOTIC MATURE SIZE BECAUSE NUMBER OF CAPILLARIES SCALES DIFFERENTLY THAN THE NUMBER OF CELLS SO GROWTH RATE CAN VANISH

⇒ DERIVE GROWTH CURVE WITH PARAMETERS DETERMINED

(1a)





GENERAL MODEL FOR GROWTH ①

HOW DOES SIZE CHANGE WITH TIME?

GOVERNED BY ENERGY UTITILISATION :

CONSERVATION OF ENERGY IN THE NETWORK :

$$B = N_c B_c + E_c \frac{dN_c}{dt}$$

B: INCOMING ENERGY (MET. RATE)

N_c: TOTAL NUMBER OF CELLS

$E_c \frac{dN_c}{dt}$: ENERGY NEED TO CREATE A CELL

$$= \text{MAINTENANCE} + \text{GROWTH}$$

$m(t)$ = TOTAL MASS OF ORGANISM AT TIME t

$$B_0 m^{3/4} = \left(\frac{m}{m_c}\right) B_c + \frac{E_c}{m_c}\frac{dm}{dt} \qquad \left[N_c = \frac{m}{m_c}\right]$$

$$\therefore \frac{dm}{dt} = \left(\frac{B_0 m_c}{E_c}\right) m^{3/4} - \left(\frac{B_c}{E_c}\right) m$$

$\left(\frac{B_0 m_c}{E_c}\right) = a$, $\left(\frac{B_c}{E_c}\right) = b$

$$\frac{dm}{dt} = a m^{3/4} - b m$$

$a m^{3/4}$: NUMBER OF

$b m$: NUMBER OF CELLS (N_c)

ORGANISMS REACH ASYMPTOTIC MASS, M ②

WHEN $\frac{dm}{dt} = 0 \Rightarrow a M^{3/4} = bM$

OR $M = \left(\frac{a}{b}\right)^4 = \left(\frac{B_0 m_c}{B_c}\right)^4$

THIS ONLY OCCURS BECAUSE $N_N \neq N_c$ IF THEY SCALED IN THE SAME WAY (i.e. $N_N \propto N_c$) THEN ALL ORGANISMS WOULD CONTINUE TO GROW THROUGHOUT ONTOGENY

REWRITE AS

$$\frac{dm}{dt} = a m^{3/4}\left[1 - \left(\frac{m}{M}\right)^{1/4}\right]$$

ASIDE: VON BERTALANFFY'S EQ^{N}

$$\frac{dm}{dt} = A m^{2/3}\left[1 - \left(\frac{m}{M}\right)^{1/3}\right]$$

NO FUNDAMENTAL BASIS]

WE TAKE E_c, B_0, m_c CONSTANTS POSSIBLY DEPENDING ON TAXONOMIC GROUP AND

$R = R_0(M)$ - SPECIES DEPENDENT

SOLUTION : ③

$$\left(\frac{m}{M}\right)^{1/4} = 1 - \left[1 - \left(\frac{m_o}{M}\right)^{1/4}\right] e^{-at/4M^{1/4}}$$

WHERE m_o = MASS AT BIRTH ($m = m_o$ WHEN $t = 0$)

a) FOR SMALL TIMES $t << \frac{4m_o^{1/4}}{a}$; $m \approx e^{kt}$ PURE EXPONENTIAL

WHERE $k = a\left[\frac{1}{m_o^{1/4}} - \frac{1}{M^{1/4}}\right]$

FOR A RAT, $\frac{4m_o^{1/4}}{a} \approx 30$ DAYS

COW, ≈ 1 YEAR

b) FOR LARGE TIMES $t >> \frac{4M^{1/4}}{a}$

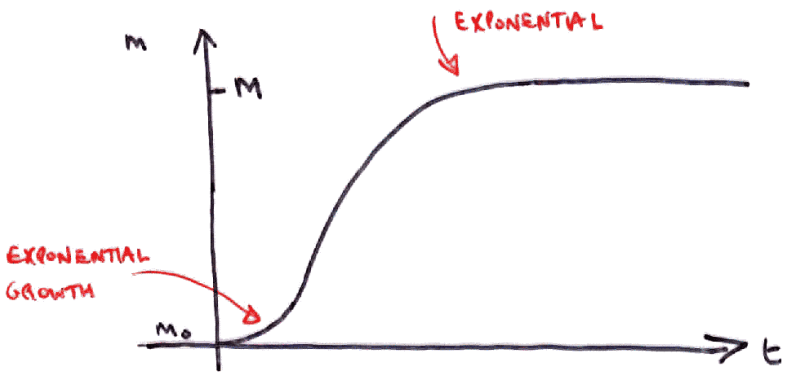
$$M - m \approx M e^{-(a/4M^{1/4})(t - t_o)}$$ PURE EXPONENTIAL

WHERE $t_o = \frac{4M^{1/4}}{a} \ln 4\left\{1 - \left(\frac{m_o}{M}\right)^{1/4}\right\}$

RAT : $\frac{4M^{1/4}}{a} \sim 130$ DAYS

COW $\sim 2\frac{1}{2}$ YEARS

④



DATA FOR MAMMALS $\Rightarrow a \sim 0.3\ g^{1/4}/\text{DAY}$

[RABBIT 0.35 ; RAT 0.23 ; COW 0.27 , PIG 0.31 , ...]

PREDICT : $a = \frac{B_o m_c}{E_c}$

$B_o \approx 1.9 \times 10^{-2}$ WATTS

$m_c \approx 3 \times 10^{-9}$ g.

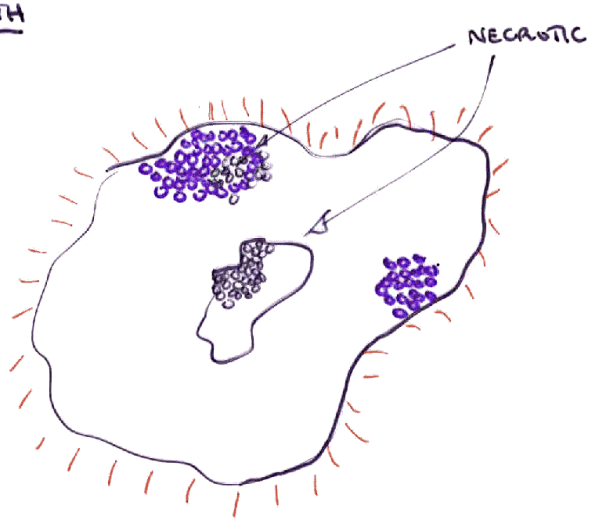
ESTIMATE E_c FROM ENERGY CONTENT OF MAMMALIAN TISSUE : MEASURED TO BE 7×10^6 J/Kg

$\Rightarrow E_c \approx 7 \times 10^6$ J/kg $\times$ 3×10^{-12} kg

$\approx 2.1 \times 10^{-5}$ J

$\rightarrow a \approx 0.25\ g^{1/4}/\text{DAY}$ IN GOOD AGREEMENT

TUMOUR GROWTH



$$B = N_c B_c + E_c \frac{dN_c}{dt}$$

ENERGY SUPPLIED BY HOST CAPILLARIES AT TUMOUR SURFACE

$$\Rightarrow B_t \approx b_1 \frac{M_t^{2/3}}{M^{1/4}} = \frac{m}{m_c} B_c + E_c \frac{dm}{dt}$$

[M_t = TOTAL TUMOUR MASS

M = VIABLE TUMOUR MASS

$M_N = M_t - M$ = NECROTIC TUMOUR MASS]

$$\Rightarrow \frac{dm}{dt} = \left(\frac{b_1}{E_c M^{1/4}}\right) M_t^{2/3} - \left(\frac{B_c}{E_c m_c}\right) m \qquad \left(\text{NOTE: } \frac{dm}{dt} \propto \frac{1}{E_c}\right)$$

BRANCHING PATTERN:

$$l_k = l_N n^{a(N-k)} \qquad \text{SPACE-FILLING} \quad a = 1/3$$

$$r_k = r_N n^{b(N-k)} \qquad \text{IF OPTIMISED (NON-PULSATILE)} \quad b = 1/3$$

BLOOD VOLUME: $V_b \propto m$ (NOT M_t!)

$$\Rightarrow B_t \propto m^{1/(a+2b)} \propto M_t^{2/3}$$

IE. $m \propto M_t^{2/3(a+2b)}$

ADDITIONALLY: $\frac{dN_c^d}{dt} = \gamma N_c \Rightarrow \frac{dm_t^d}{dt} = \gamma m$

DETERMINES M_N

$\Rightarrow b \sim 1/6$

COMPARE / CONTRAST:

HEALTHY ONTOGENY

FETUS

TREES / PLANTS

TUMOURS

DEAD TISSUE, NON-PULSATILE, SMALLER E_c, ...

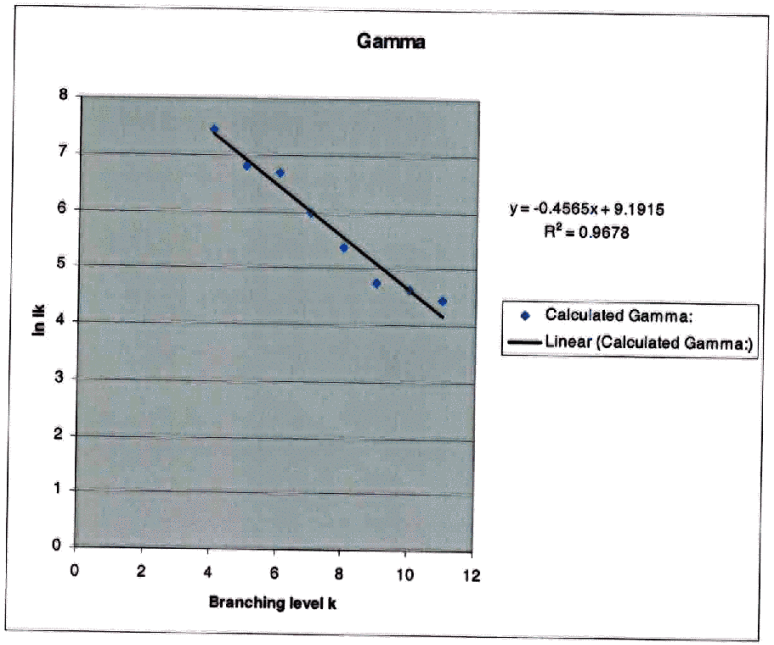


Figure Error! No text of specified style in document.**-1 A semi log plot of vessels lengths versus branching order *k*, with $\gamma = .6335$. Data adapted from [78].**

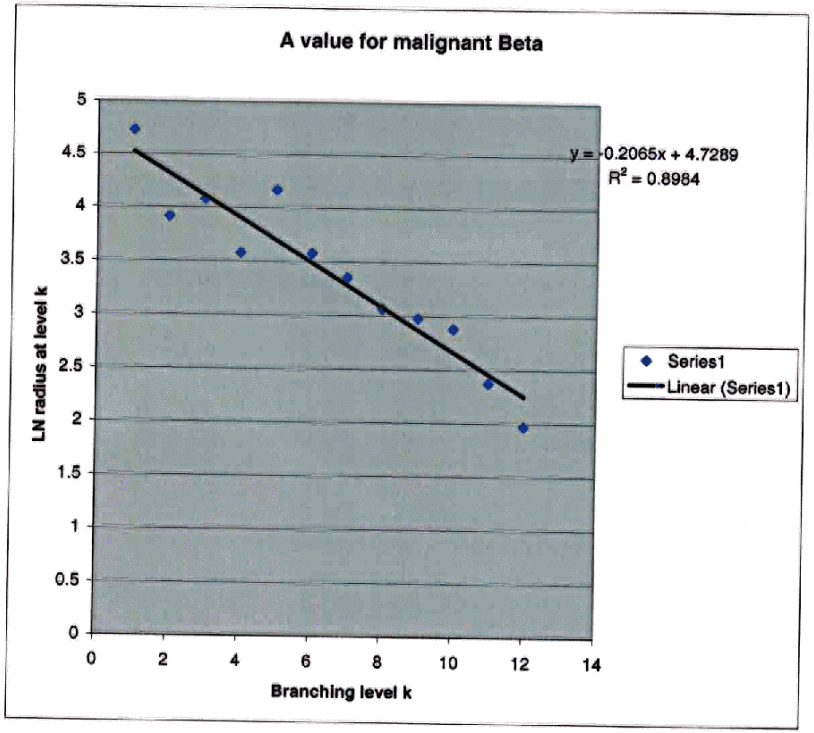
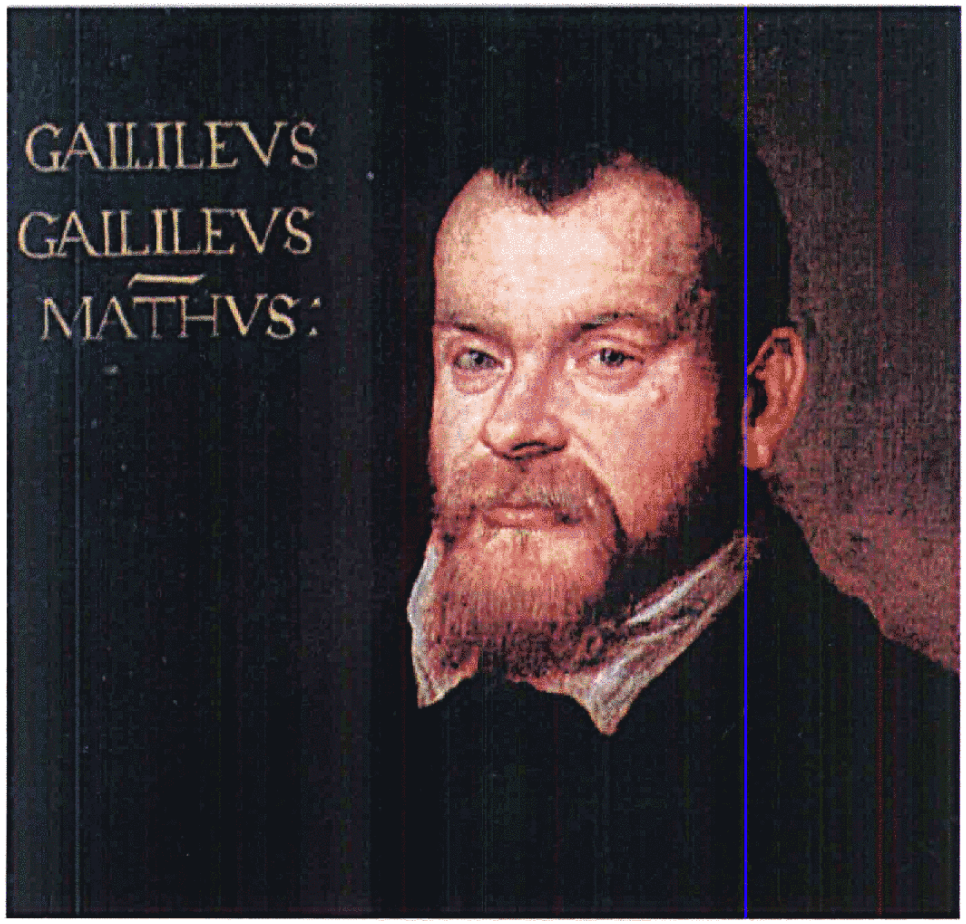
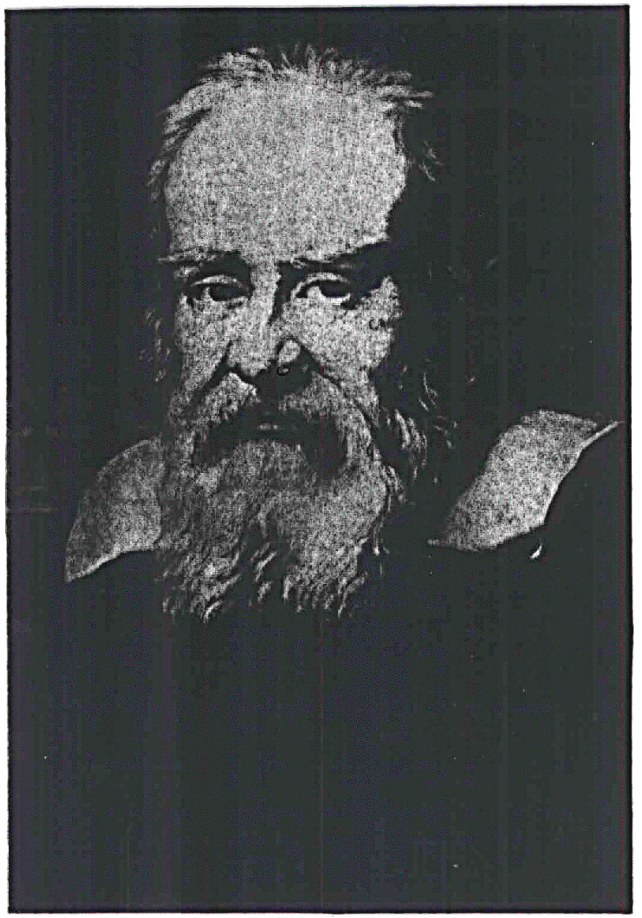


Figure Error! No text of specified style in document.**-1 A value for malignant β for mammary carcinoma. $\beta = e^{-.2056} = .8134, R^2 = .8984$. Data adapted from [78].**





GALILEO GALILEI.
Subterman's portrait, painted about 1640; now in the "Galleria de' Pitti" at Florence.

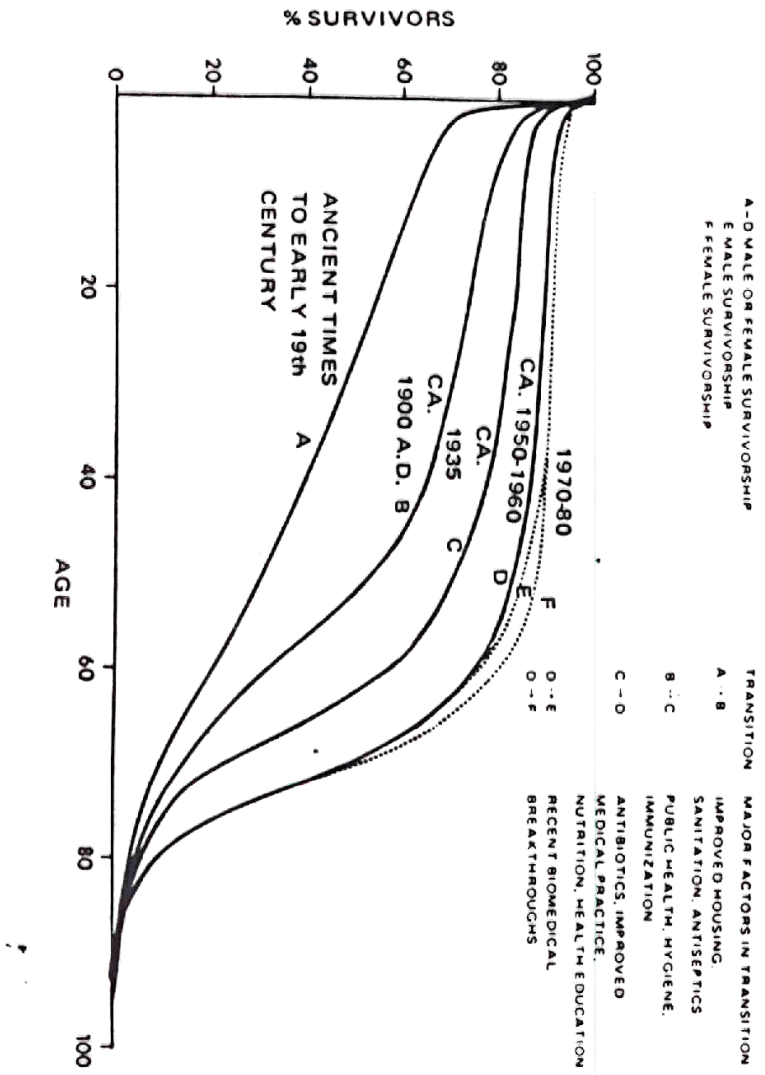


TABLE 1. Gain in Expectancy of Life at Birth and at Age 65 Due to Elimination of Various Causes of Death[a]

Cause of Death	Gain in Expectancy of Life (Yrs) if Cause Was Eliminated	
	at Birth	at Age 65
Major cardiovascular-renal	10.9	10.0
Heart disease	5.9	4.9
Vascular diseases affecting central nervous system	1.3	1.2
Malignant neoplasms	2.3	1.2
Accidents other than by motor vehicle	0.6	0.1
Motor vehicle accidents	0.6	0.1
Influenza and pneumonia	0.5	0.2
Infectious diseases (excluding tuberculosis)	0.2	0.1
Diabetes mellitus	0.2	0.2
Tuberculosis	0.1	0.0

[a] From life tables published by the National Center of Health Statistics.[18]

i) BEGIN DYING AS SOON AS YOU FINISH GROWING

ii) UNIFORM PHENOMENON

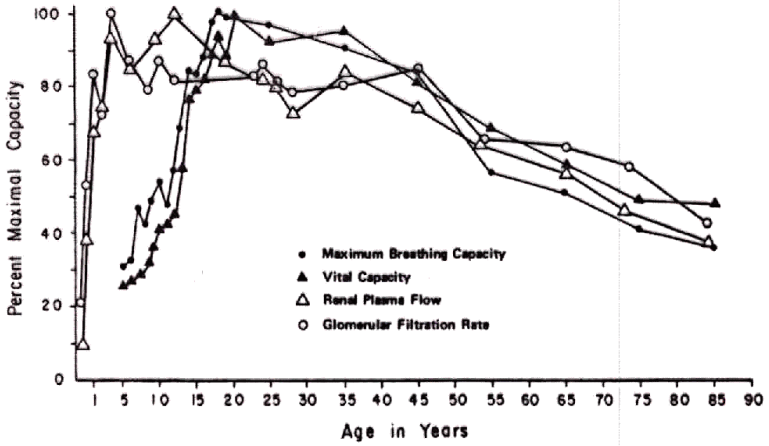


FIGURE 2. Change in organ function with age. (From Bafitis & Sargent.[17] Reprinted by permission from the *Journal of Gerontology*.)

"THOSE NOT BUSY BEING BORN ARE BUSY DYING:"

AGING AND MORTALITY - SPECULATIONS

I. OBSERVATIONS / ASSUMPTIONS

i) AGING AND DEATH ARE UNIVERSAL AMONG ORGANISMS

ii) AGING IS APPROXIMATELY UNIFORM IN INDIVIDUAL

iii) THERE IS AN ASYMPTOTIC SURVIVAL RATE AND CORRESPONDING MAXIMUM LIFESPAN (MAX, MEAN, ...)

iv) LIFESPAN $T \sim M^{1/4}$

MAMMALS: $\frac{T}{T_0} \approx \left(\frac{M}{M_0}\right)^{1/4}$ $M_0 = 1\,kg$, $T_0 \approx 10\,yrs$

v) TOTAL NUMBER OF HEARTBEATS / CYTOCHROME O IS INVARIANT

(2)

II. QUEST : QUANTITATIVE THEORY OF MORTALITY

(ANALOGOUS TO THEORY OF GROWTH)

WOULD LIKE TO EXPLAIN ORIGIN OF SCALING LAW AND ITS NORMALISATION SCALE

WHY DO WE LIVE FOR THE ORDER OF 100 YEARS AND NOT A MILLION OR JUST A FEW MONTHS ?

(IE. WHY IS $T_0 \sim 10$ YEARS)

HOW DOES THE SCALE OF 10 OR 100 YEARS COME FROM MICROSCOPIC (MOLECULAR) SCALES ?

(3)

III. MODEST SPECULATIVE RESPONSE

WE HAVE A THEORY OF HOW LIFE IS SUSTAINED

[HIERARCHICAL BRANCHING NETWORK SYSTEMS

⇒ THEORY OF GROWTH]

HOWEVER, THESE SYSTEMS ARE TYPICALLY

DISSIPATIVE : "FRICTIONAL" FORCES CREATE ENTROPY AND ENERGY DAMAGING MOLECULES

HYPOTHESIS : THIS CONTINUOUS DAMAGE RELENTLESSLY DEGRADES THE SYSTEM (IN SPITE OF REPAIR MECHANISMS) LEADING INEVITABLY TO AGING AND DEATH !

CAN WE MAKE THIS QUANTITATIVE ?

④

IV. THE IDEA

MOST VULNERABLE PARTS OF SYSTEM ARE THE TERMINAL UNITS – ALSO MOST IMPORTANT – WHERE SUSTAINING METABOLIC ENERGY IS EXCHANGED WITH THE ENVIRONMENT (INTERNAL OR EXTERNAL)

BECAUSE THEY ARE THE SMALLEST, THEY SUSTAIN THE GREATEST DISSIPATIVE FORCES

"DEATH" OCCURS WHEN A MACROSCOPIC NUMBER (SOME GIVEN PERCENTAGE OF THE TOTAL) OF FUNDAMENTAL UNITS (MOLECULES) HAVE BEEN (IRREPARABLY) DAMAGED (N)

DAMAGE OCCURS VIA INELASTIC COLLISIONS WHICH SIGNIFICANTLY ALTER THESE UNITS

⑤

IF EACH SUCH DAMAGING COLLISION REQUIRES AN ENERGY ΔE AND dE/dt IS THE RATE OF ENERGY DISSIPATION THEN DEATH OCCURS WHEN

$$T \frac{dE}{dt} \approx N \Delta E$$

I.E. SYSTEM CANNOT CONTINUE FUNCTIONING FOR TIMES $t > T$ WHERE

$$T \sim \frac{N \Delta E}{dE/dt}$$

SOME SCALES

i) $\Delta E \sim$ eV (QED)

$\sim 5 \times 10^{-19}$ J. (MOLECULAR ENERGY)

ii) $N \propto M \sim$ AVAGADRO'S NUMBER $\sim 10^{24}$

iii) $B \sim$ 100 watts = 100 J/sec

iv) POWER EXPENDED BY HEART $\sim$ 1 watt

(6)

GENERALLY,

$$\frac{dE}{dt} \approx N_N \frac{dE_N}{dt}$$

N_N: NUMBER OF TERMINAL UNITS

$\frac{dE_N}{dt}$: ENERGY DISSIPATED IN EACH TERMINAL UNIT

NOW: $N_N \propto M^{3/4}$

AND $\frac{dE_N}{dt} \propto M^0$

BUT $N \propto M$ AND $\Delta E \propto M^0$

$\Rightarrow T \propto M^{1/4}$

NOTE: IF $N_N \propto M$, THEN $T \propto M^0$ AND ALL ORGANISMS WOULD LIVE SAME LIFESPAN

(RECALL: THIS WOULD ALSO IMPLY THEY WOULD CONTINUE GROWING INDETERMINATELY)

(7)

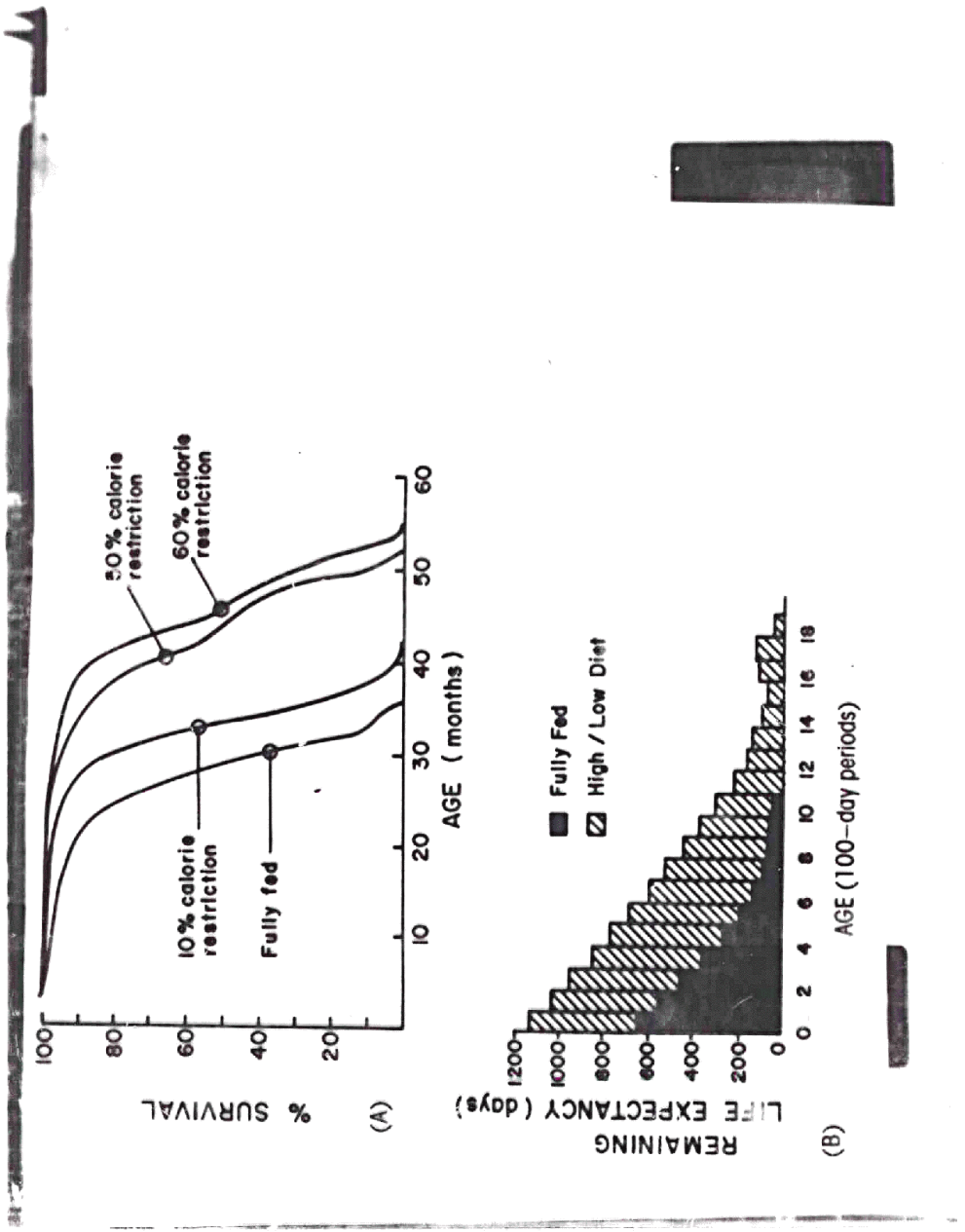
MOST OF METABOLIC ENERGY IS DISSIPATED IN THE CAPILLARY SYSTEM OF THE CIRCULATORY SYSTEM

DAMAGING COLLISIONS ONLY TAKE PLACE IN A BOUNDARY LAYER OF THICKNESS δ:

$$\frac{dE_N}{dt} \approx \frac{\pi (\Delta p)^2 r_N^3}{4 \mu \ell_N} \delta \qquad \left[\frac{\delta}{r_N} \sim 0.05\right]$$

$\Rightarrow T \sim 50$ YEARS (ACCIDENT!)

INTERPLAY BETWEEN VERY SMALL NUMBERS CHARACTERISING MOLECULAR SCALES AND VERY BIG NUMBERS CHARACTERISING SIZE OF ORGANISM


% SURVIVAL
100
80
60
40
20
10
20
30
40
50
60
AGE (months)
50% calorie restriction
60% calorie restriction
10% calorie restriction
Fully fed
(A)
REMAINING LIFE EXPECTANCY (days)
1200
1000
800
600
400
200
0
0 2 4 6 8 10 12 14 16 18
AGE (100-day periods)
Fully Fed
High / Low Diet
(B)