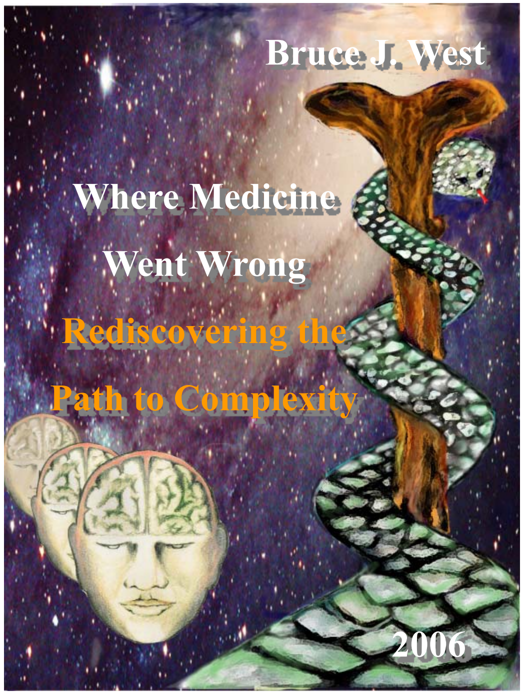


A Medical Tale of Tails:
Applications and Implications of Inverse Power Laws in Primary Care Research

at

Primary Care Research Methods & Statistics Conference

San Antonio, TX

January 22, 2010

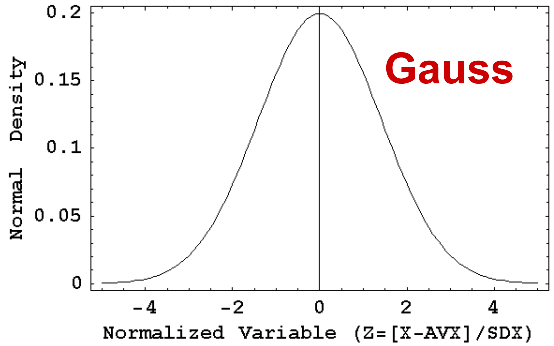
Collaborators:

Paolo Grigolini
Mirek Latka
Elliott Montroll
Jonas Salk

Bruce J. West
Mathematical & Information Sciences Directorate
Army Research Office
Research Triangle Park, NC

Some things we will discuss

- **Physical and Physiological laws involve averages**

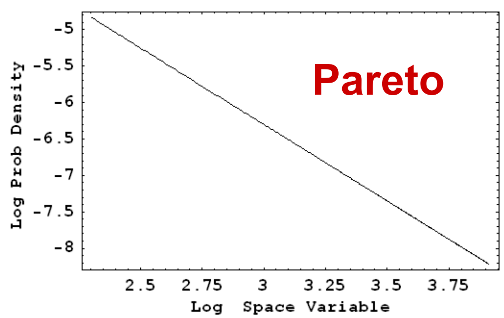


mean dominates

fluctuations are normal

central limit theorem

- **Complexity implies inverse power law**
  - **examples from social, physical and life sciences**



- **Inverse power laws imply fractal phenomena**
  - **geometrical**
  - **statistical**

scaling **?** **medicine**

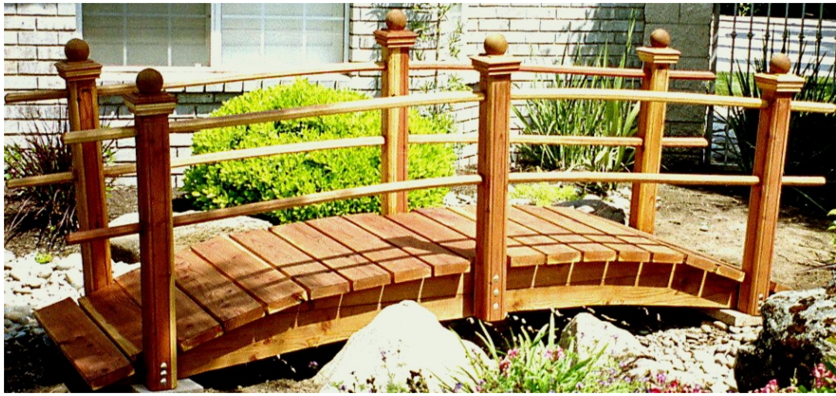
Historically complexity was modeled using statistics

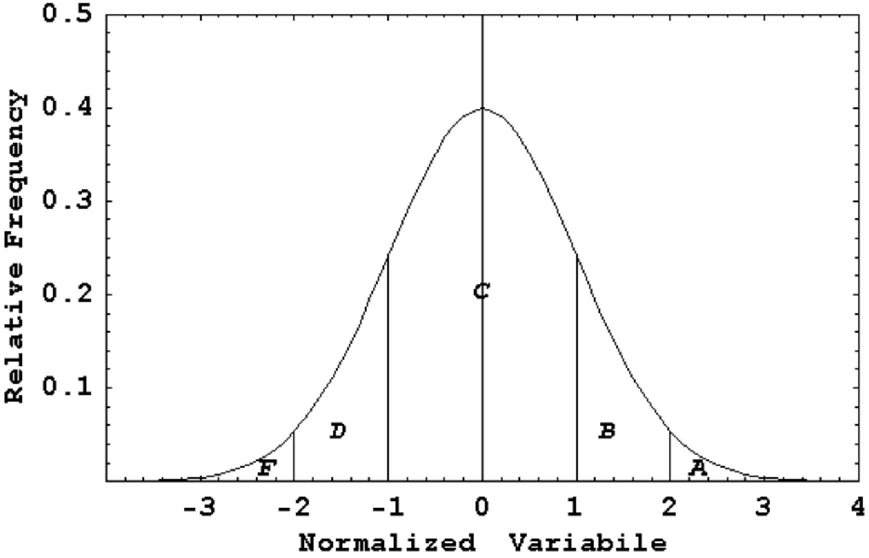
- **Gauss**
  - **simple processes; twinkle twinkle little star**
  - **permeated social and life science of 19th century**
  - **bell-shaped distribution**
  - **lead to ‘average man’**

- **Pareto**
  - **complex processes; solar flares and sun spots**
  - **gained traction in last half of 20th century**
  - **inverse power-law distribution**
  - **vital few**

Normal (Gauss) world view

- **Linear**
  - **simple rules yield simple results**
  - **things are additive**
  - **output is proportional to input**
  - **predictable**
  - **normal distribution**



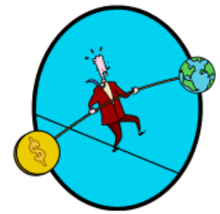


- **Every student knows its true; but where is the evidence?**

Averages & rates represent phenomena

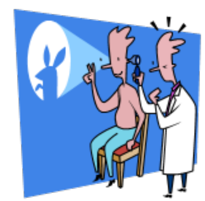
- heart rate

balance



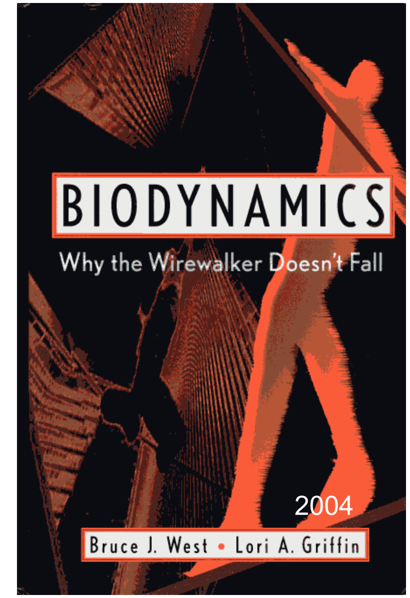
- stride rate

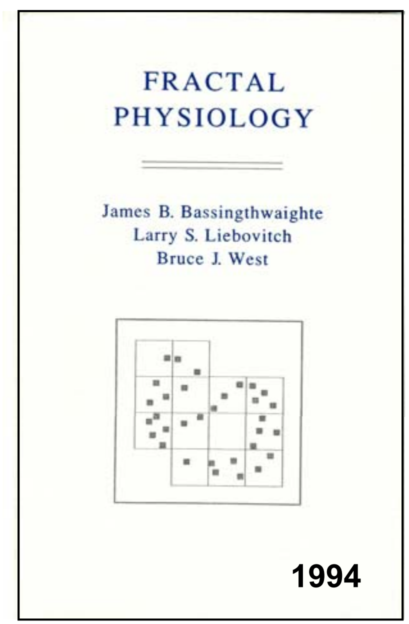
cerebral blood flow



- breathing rate

circadian rhythm





How do we know this is true?

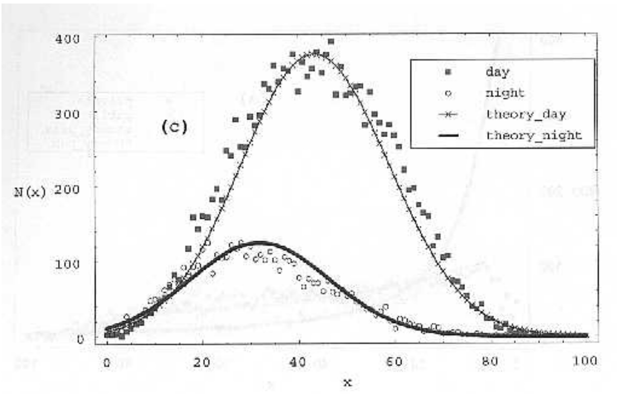
Data source

• **University entrance examination of Universidade Estadual Paulista (UNESP) in state of Sao Paulo, Brazil: Gupta, Campanha & Chavorette, *Int. J. Mod. Phys*. 2004**

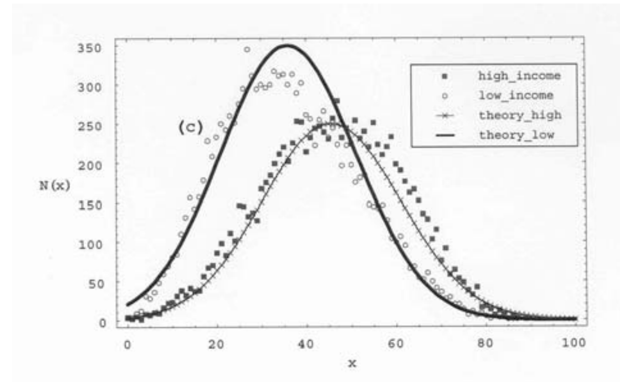
• **data for approximately 60,000 students graduating high school and taking entrance examination**

Humanities

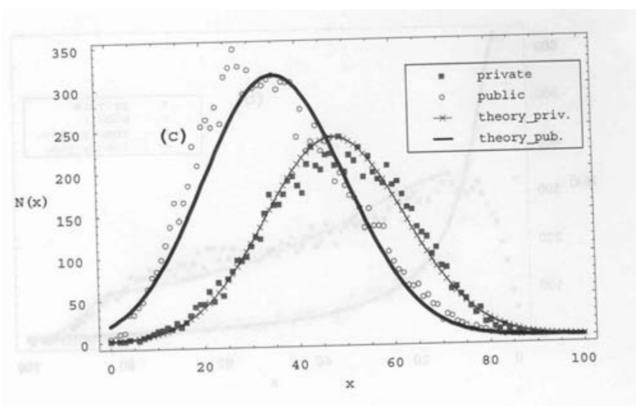
day & night students (2000)



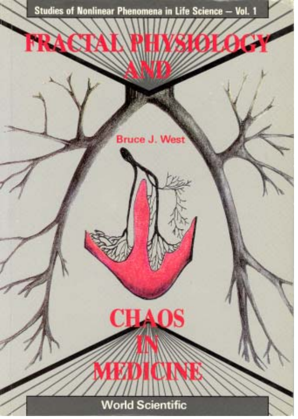
high & low income (2000)



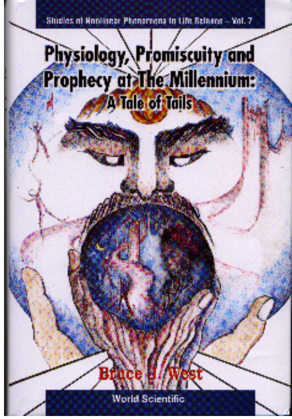
private & public students (2000)



Gauss was right!



Not necessarily Gauss



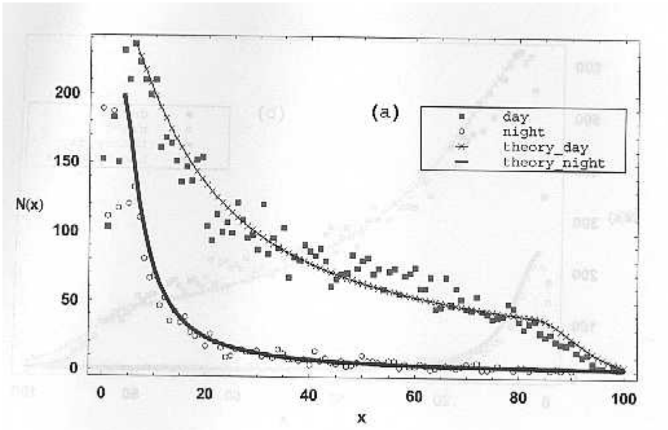
H. Poincaré (1854-1912):

"All the world believes it firmly, because the mathematicians believe it is a fact of observation and the observers believe it is a theorem of mathematics."

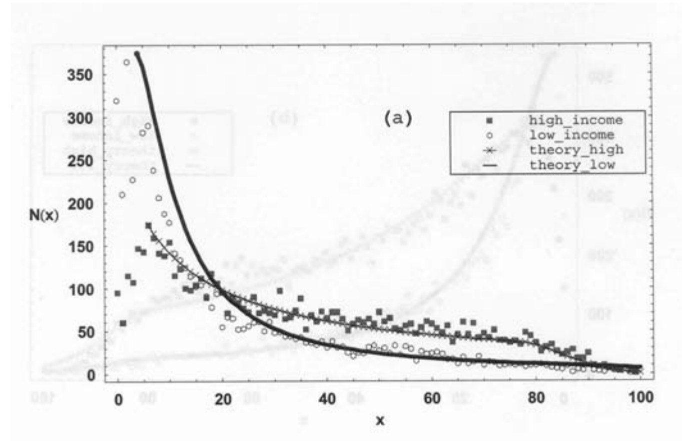
So we look at more data!

Physical Sciences

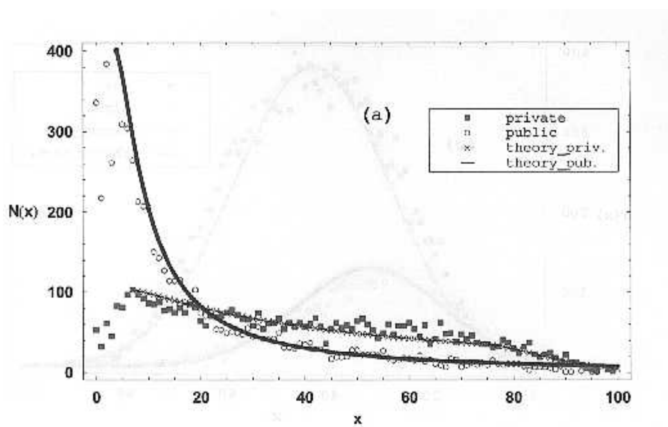
day & night students (2000)



high & low income students (2000)



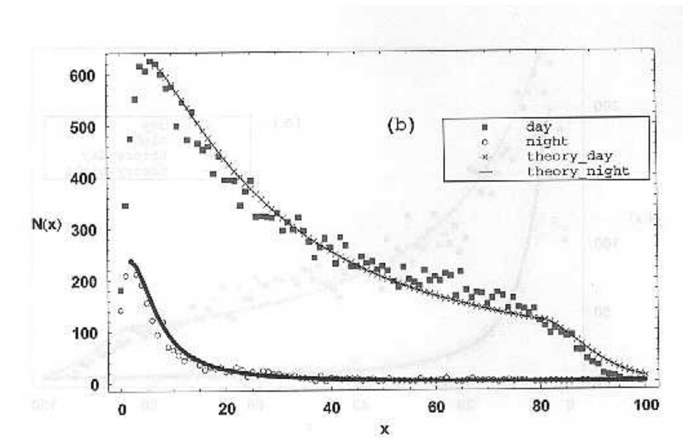
private & public students (2000)



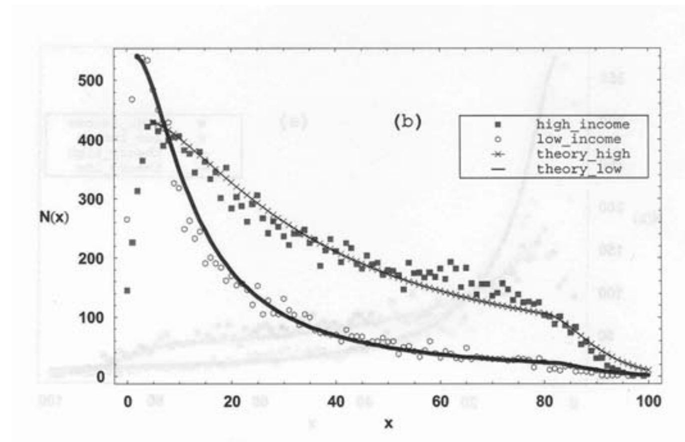
Not bell-shaped !

Biological Sciences

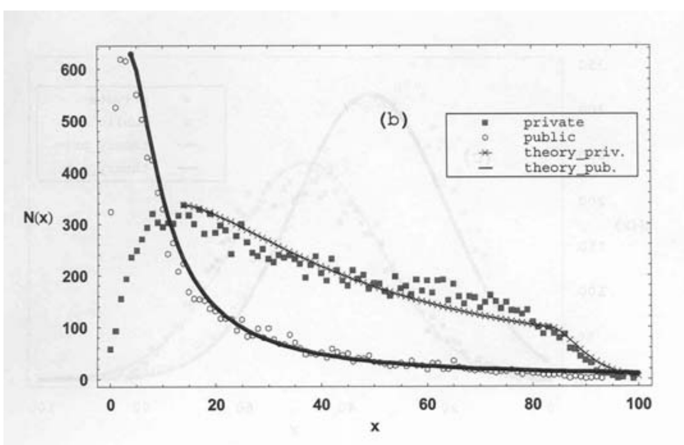
day & night students (2000)



high & low income students (2000)



private & public students (2000)



Not bell-shaped either !

What happened to Gauss?

- **Humanities consists of many disjoint subjects:**
  - **history, language, philosophy, social studies and so on**
  - **satisfies condition for the normal (Gauss) distribution**

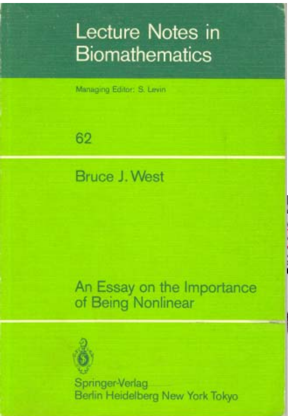
- **Physical sciences are based on sequential interdependent studies:**
  - **elementary science**
  - **basic mathematics through algebra and trigonometry**
  - **calculus**
  - **physics**
  - **chemistry**

- **Biological sciences are also based on sequential interdependent studies**

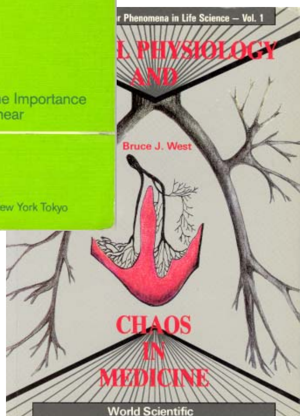
- **Interdependence and memory are complex, violating the conditions for Gauss distribution.**

Inverse power-law distribution replaces Gauss!

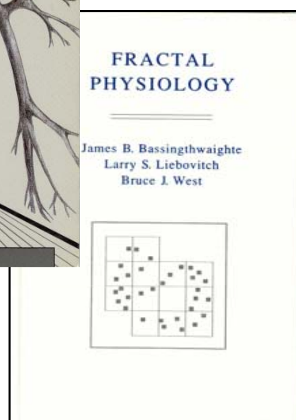
1985



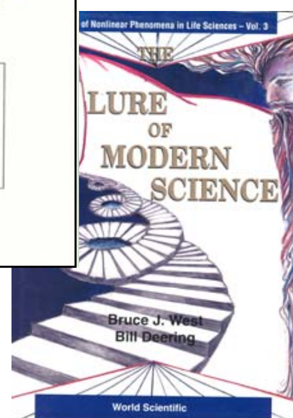
1990



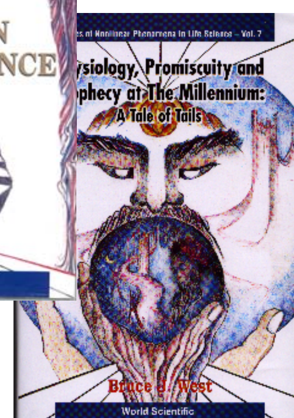
1994



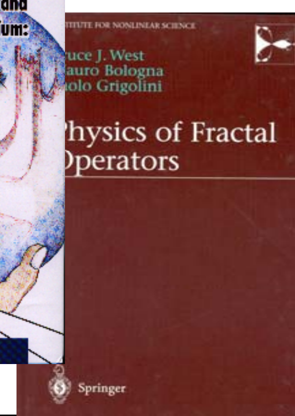
1995



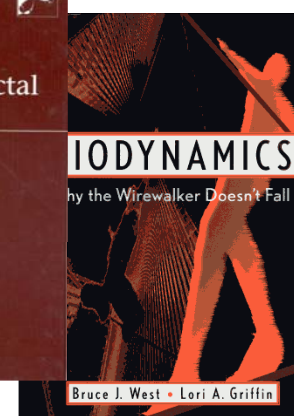
1999



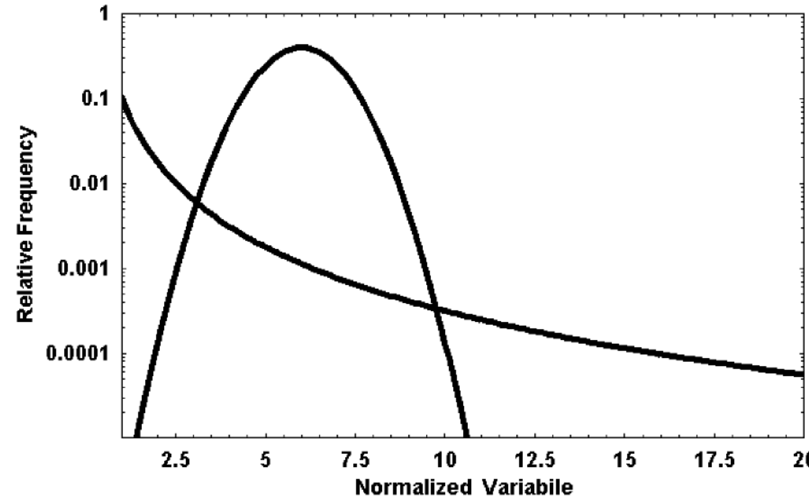
2003



2004



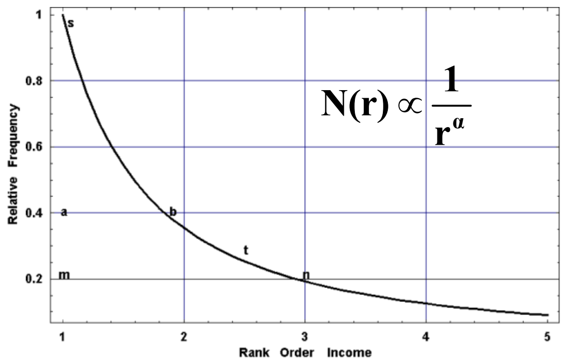
2006



What is the evidence?

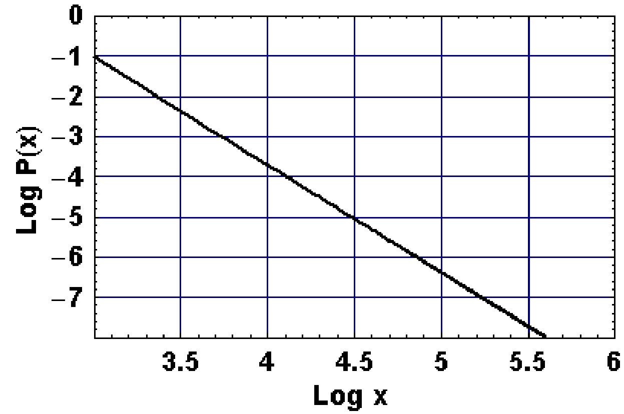
Pareto's Law

Vilfredo Pareto, *Cours d'Economie Politique* (1896).

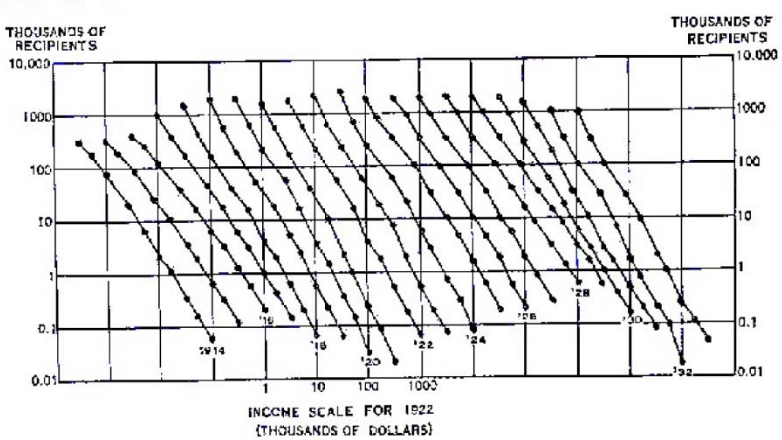


Log-log transformation

$$\log P(x) = -\alpha \log x + \text{const.}$$

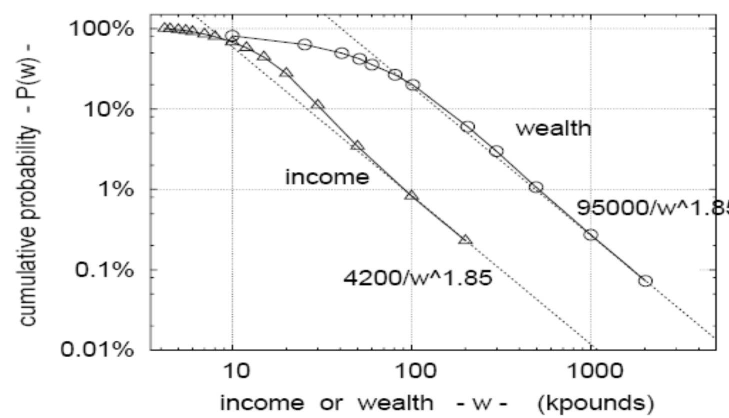


Income distribution in United States ('14-'33)



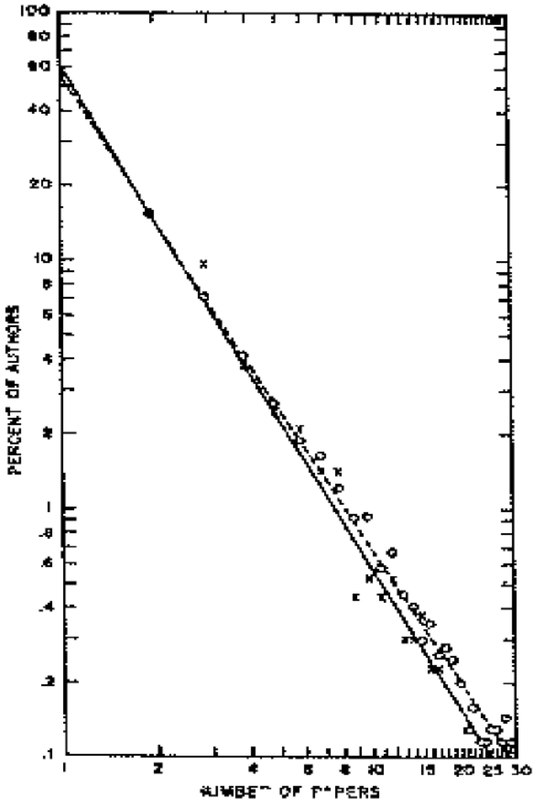
Income is a complex process

- **Society is not fair; UK 2005**



Lotka's Laws

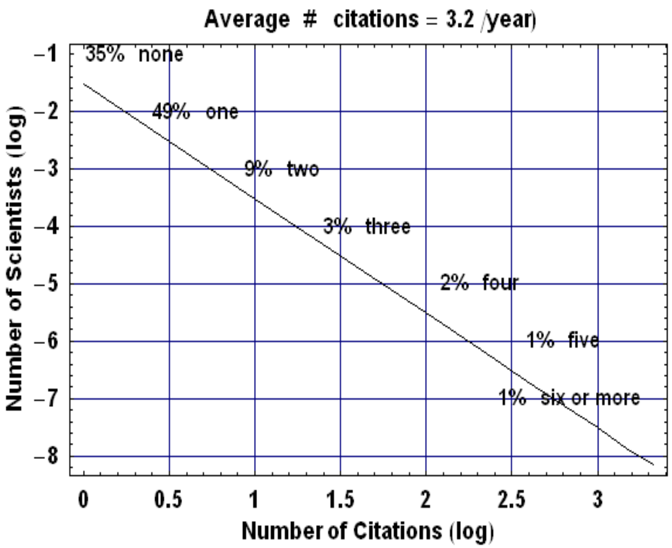
Alfred J. Lotka,
***Elements of Mathematical Biology* (1924)**



- **de Solla Price**
  Little Science,
  ***Big Science* (1963)**

$$P(x) \propto \frac{1}{x^3}$$

Number of citations



- **96% of all scientists publish less than the average**

- **Are you average?**

Publishing papers is a complex process

40 'NATURAL' INVERSE POWER-LAW NETWORKS

- sand pile avalanches
- fracture of materials
- brush-fire damage
- flooding of Nile
- laser technology evolution
- hurricanes and floods
- earthquakes
- power system blackouts
- coastlines
- magma rising through earth's crust
- punctuated equilibrium
- asteroid hits
- mass extinctions/explosions
- sun spots
- galactic structure
- frequency of DNA base chemicals
- genetic circuitry
- protein-protein interactions
- metabolism of cells
- neural network branching
- cellular substructures
- magnitude estimate of sensorial stimuli
- circulation in plants and animals
- phytoplankton
- number vs. size of plant genera
- brain functioning
- tumor growth
- fetal lamb breathing
- bronchial structure
- heartbeats
- predicting premature births
- functional networks in brain
- density-dependent regulation of plants
- species abundance
- biodiversity
- body size of species
- epidemics
- predators food source
- size distribution in ecosystems
- mass extinctions

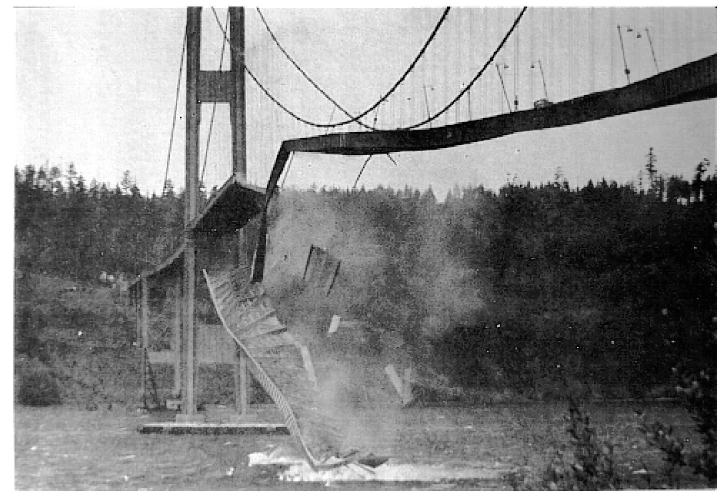
40 'SOCIAL' INVERSE POWER-LAW NETWORKS

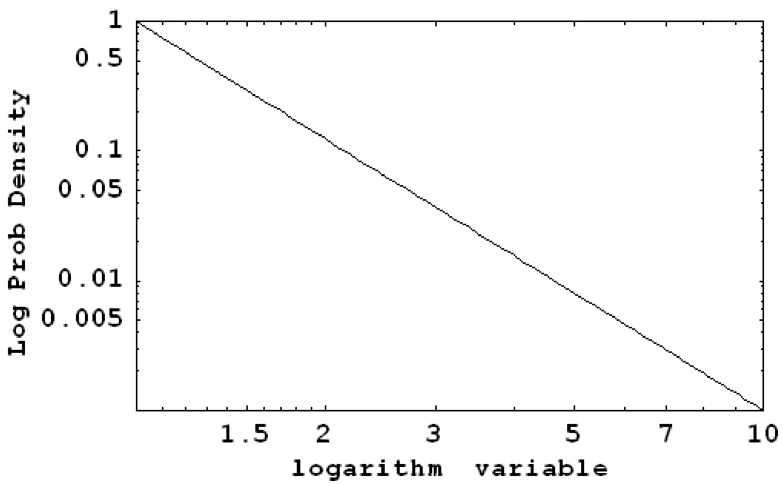
- language – word usage
- social networks
- blockbuster drugs
- sexual networks
- distribution of wealth
- citations
- co-authorship
- casualties of war
- growth rate of GDPs
- delinquency rates
- movie profits
- actor networks
- size of villages
- distribution of family names
- consumer products
- copies of books sold
- number of telephone calls and emails
- deaths of languages
- aggressive behavior among children
- structure of internet equipment
- internet links
- # hits website/day
- price movements on exchanges
- economic fluctuations
- salaries
- labor strikes
- job vacancies
- firm sizes
- growth rates of firms
- growth rates of internal structure
- supply chains
- cotton prices
- alliances among biotech firms
- entrepreneurship/innovation
- director interlock structure
- Italian industrial clusters
- global terrorism events
- intra-firm decision events

Pareto World View

- **Nonlinear**
  - **simple rules yield complex results**
  - **small changes may diverge**
  - **limited predictability**
  - **inverse power-law distributions**

Tacoma Narrows Bridge Disaster 1940





- **Almost no one knows its true.**

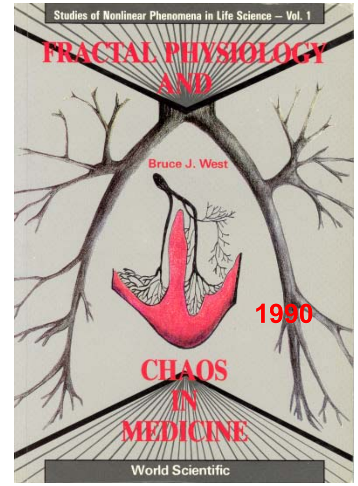
It’s not what you expected!

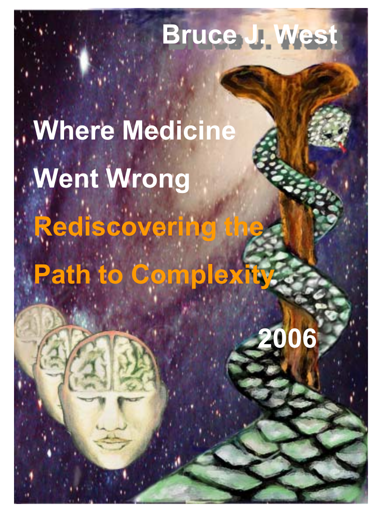
- Inverse power laws are strange:
  - most workers earn less money than average
  - most investigators publish fewer papers than average
  - most scientists are cited fewer times than average
  - most speakers use fewer words than average
  - most people live is larger cities than average
  - most EW patients stay in hospitals less time than average
  - most damage is caused by fewer failures than average
- The average never characterizes a complex phenomenon.

No Average? Then What ?

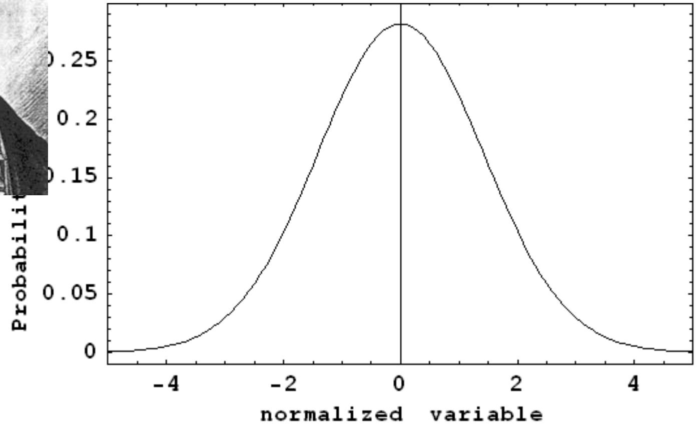
- **The slope replaces the average as the metric**
  - **slope measures the extent of imbalance**
  - **slope measures the degree of ‘unfairness’**
  - **slope measures degree of variability**
  - **slope gives fractal dimension**

- **Disease is not the loss of regularity but the loss of complexity**

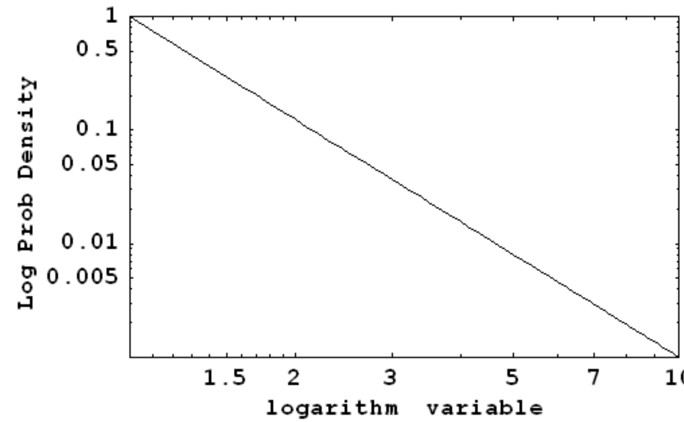




Gauss; bell curve (circa 1800)



Pareto; inverse power law (circa 1900)



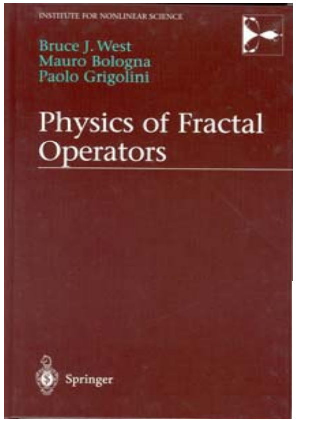
- **Simple scientific world view**
  - linear; output is proportional to input
  - additive
  - simple rules yield simple results
  - stable
  - predictable
  - quantitative
  - normal distribution
- **Complex scientific world view**
  - nonlinear; small changes may diverge
  - multiplicative
  - simple rules yield complex results
  - unstable
  - limited predictability
  - qualitative plus quantitative
  - inverse power-law distributions

Complexity ⇨ Pareto ⇨ Fractal

- **So how do fractals change our interpretations of things in the real world?**

- **Statistical fractal phenomena are very often described by inverse power laws.**

- **Fractals imply scaling.**



Self-similar structure and self-similar dynamics

Geometrical Fractal

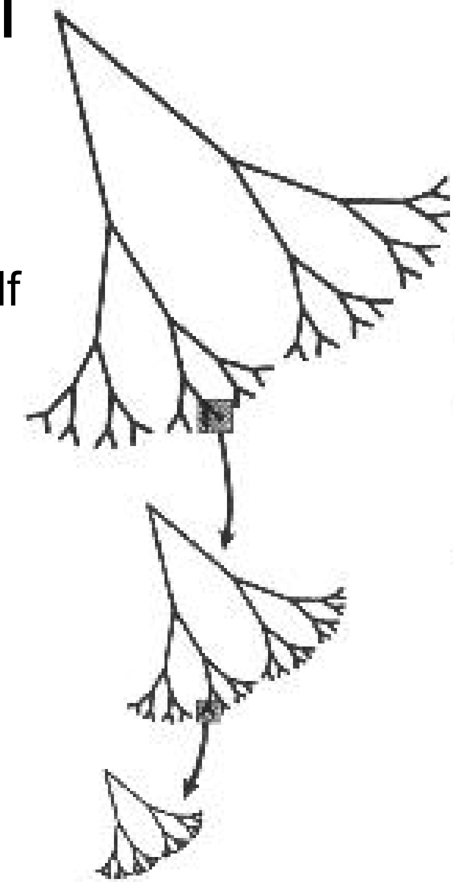
Tree-like

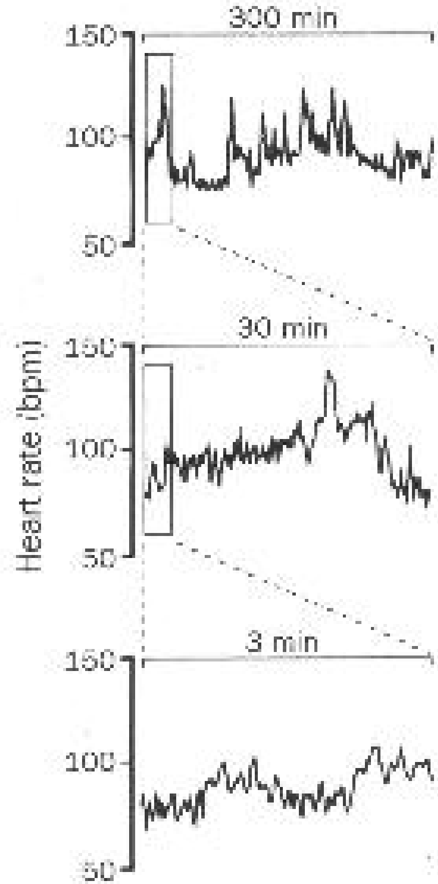
• self-similar branching

• structure repeats itself on all levels of the hierarchy

• magnify branches at each level

• branches, within branches, within branches





Statistical Fractal

Time series

• Heart rate regulation

• fluctuations are self-similar in a statistical way

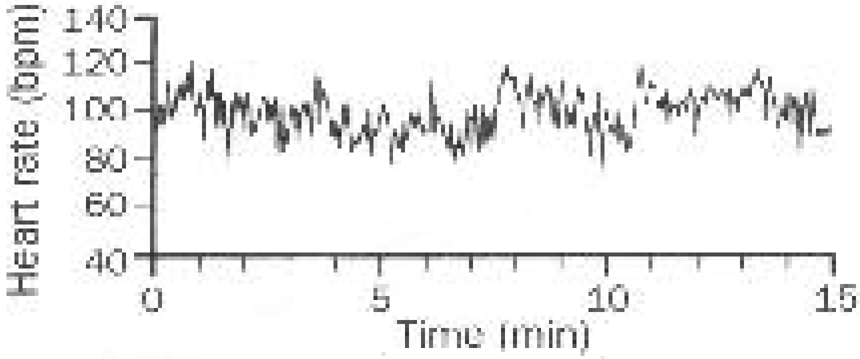
• clumps, within clumps, within clumps

$$X(\lambda t) = \lambda^{\alpha} X(t)$$

$$p(x,t) = \frac{1}{t^{\delta}}\, p\left(\frac{x}{t^{\delta}}\right)$$

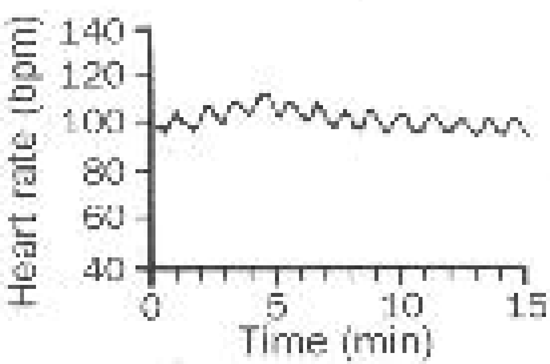
Pathological Breakdown of fractal dynamics

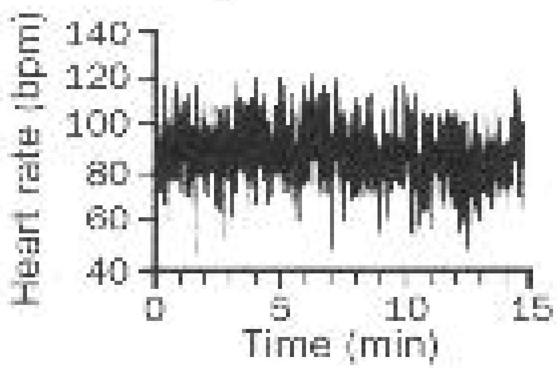
Healthy dynamics $1.1 \le D \le 1.3$



Increased correlation

Decreased correlation





Single scale – heart failure

$D \approx 1.0$

Uncorrelated randomness – atrial fibrillation

$D \approx 1.5$

- Healthy heart rate
  - **multiple scales**
  - **long-range order**
  - **fractal time series**

    (A.L. Goldberger, Lancet 347, 1312, 1996)
- Correlation index

$$r = 2^{3-2D} - 1$$

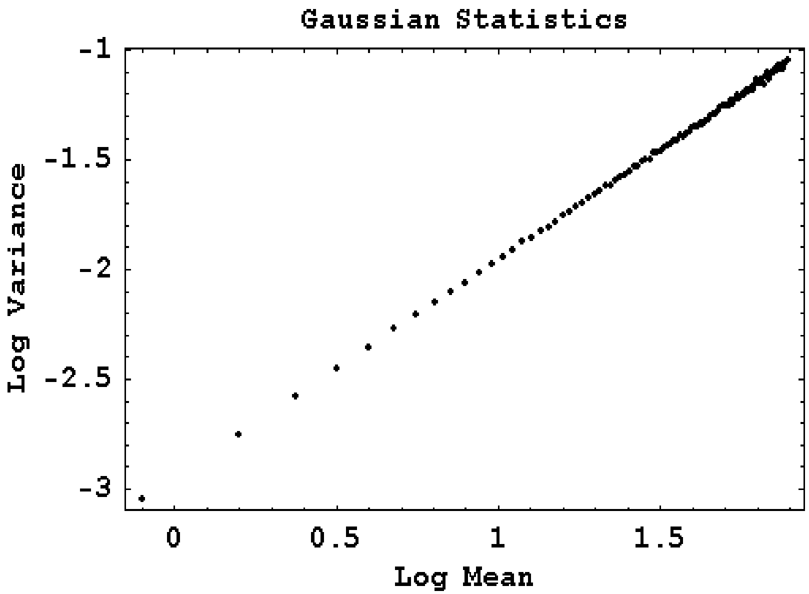
Taylor's Law, data and time series correlations

- **Power curve**

$$VarX(m) = a\overline{X}^{b}(m)$$

  - b > 1 clumped ;
  - b < 1 even ;
  - b = 1 random

- **Fractal dimension**
  - D = 2 - b/2



- **Correlation coefficient**

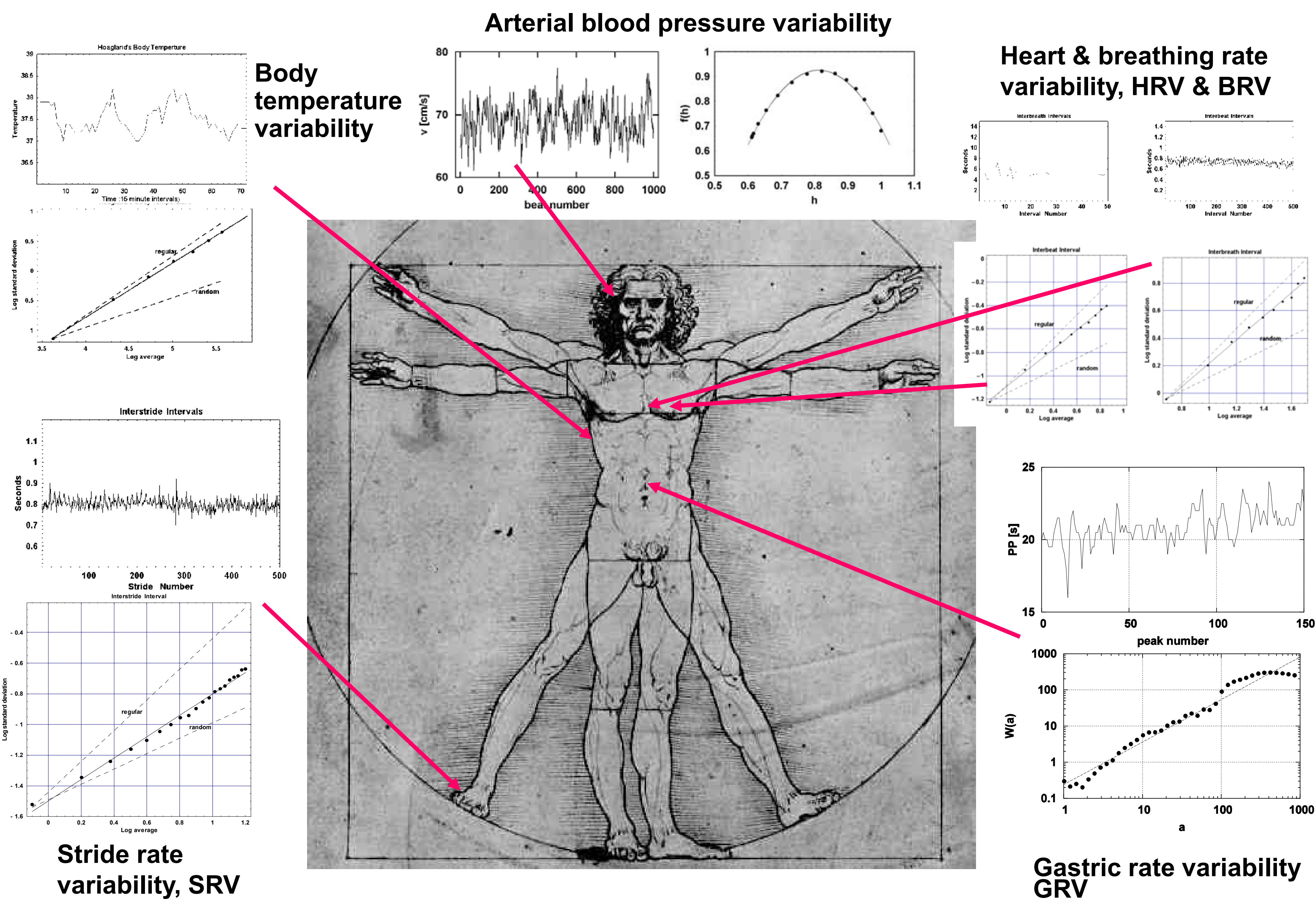
$$r = 2^{3-2D} - 1$$

r = 0 uncorrelated → D = 1.5

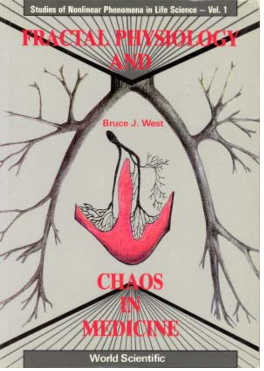
r = 1 regular → D = 1.0

$$\left\langle X(t)^2 \right\rangle \propto t^{2H} \qquad D = 2 - H$$

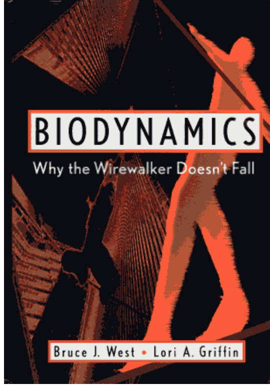
- **Computer generated data**
  - Gaussian statistics
  - Aggregated data
  - b = 1, random
  - D = 1.5


Arterial blood pressure variability
Body temperature variability
Heart & breathing rate variability, HRV & BRV
Hoagland's Body Temperture
Temperature
Time :16 minute intervals
Log standard deviation
Log average
regular
random
v [cm/s]
beat number
f(h)
h
Interbreath Intervals
Interbeat Intervals
Seconds
Interval Number
Interbeat Interval
Interbreath Interval
Interstride Intervals
Stride Number
Interstride Interval
PP [s]
peak number
W(a)
a
Stride rate variability, SRV
Gastric rate variability GRV

Conclusions



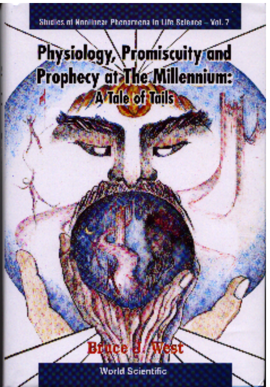
1990



2004

- **Complex phenomena are described by the statistics of Pareto not Gauss.**
- **Scaling properties indicate an underlying fractal behavior, either in the geometrical structure or in the statistics.**
- **Scaling of complex phenomena imply that scaling indices, not averages, better characterize the process.**
- **Most physiologic phenomena are complex and described by inverse power laws, so that the average is truly exceptional.**
- **Disease is loss of variability and not the loss of regularity.**

1999



2006