Fractals in Physiology

A Biomedical Engineering Perspective

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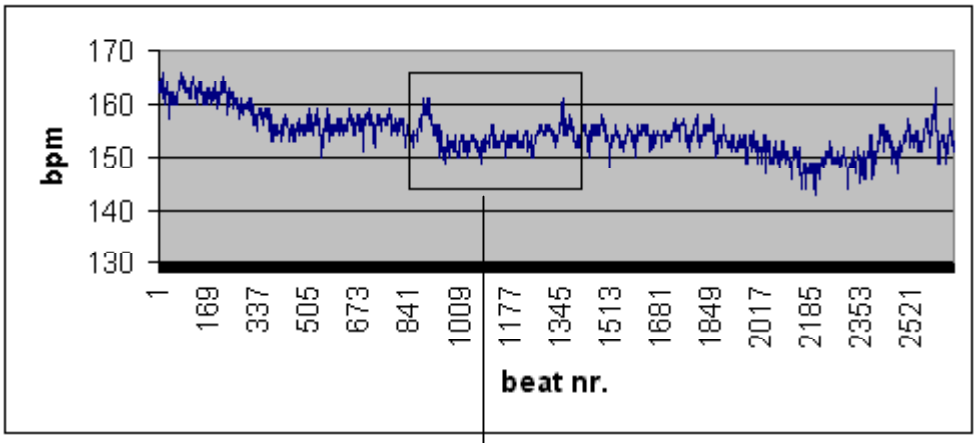
1 - MOTIVATION

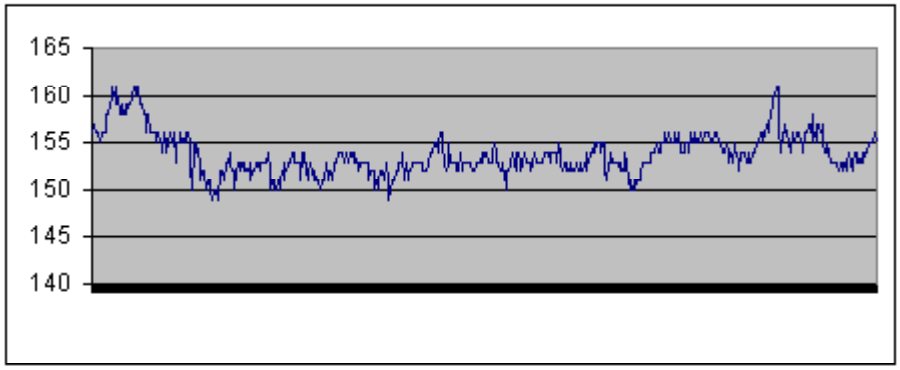
Many physiological signals exhibit almost random behaviour…

Foetal Heart Rate



C. Felgueiras, J.P. Marques de Sá (1998)

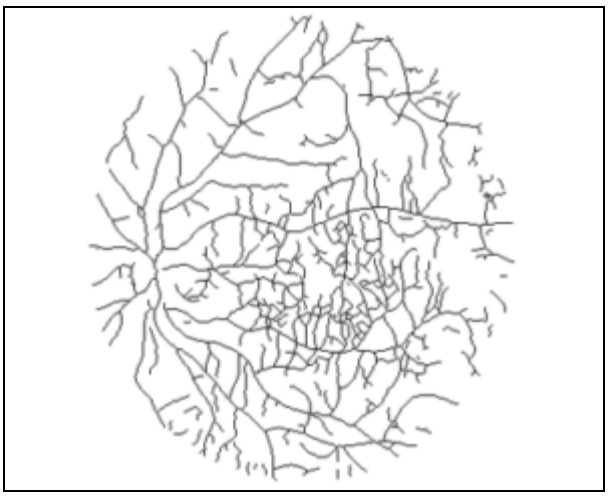
but with statistical "self-similarity"



Model: Temporal Fractal

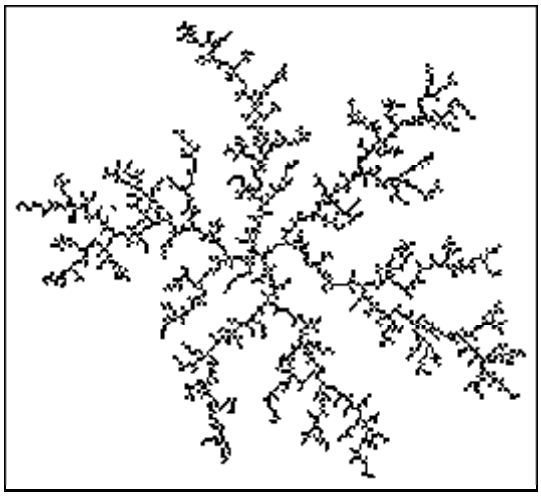
Many physiological structures exhibit a high degree of spatial complexity…

Human Retina Image



Retina angiogram. A.M. Mendonça, A. Campilho (1997)

But some "repeating" law may be present…

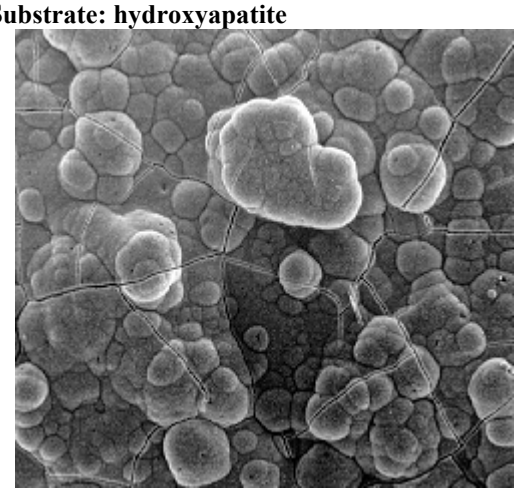


Diffusion Limited Aggregation Process: a particle falls randomly in a circle of radius *R* and diffuses until anchoring to another particle or getting out of the circle. Nr of points available for growth in a circle of radius *r*: $N(r) \approx r^D$

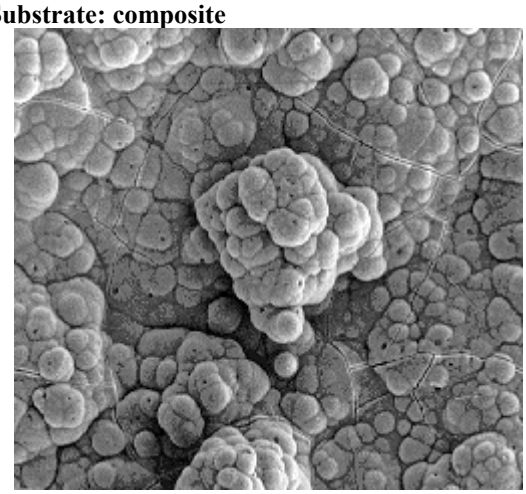
Model: Spatial Fractal

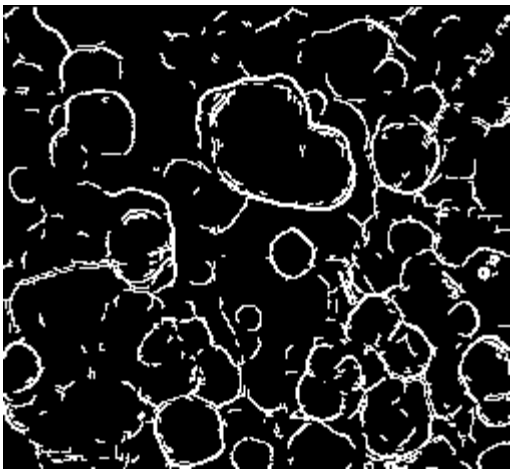
Hydroxyapatite Growth on Bioactive Surfaces

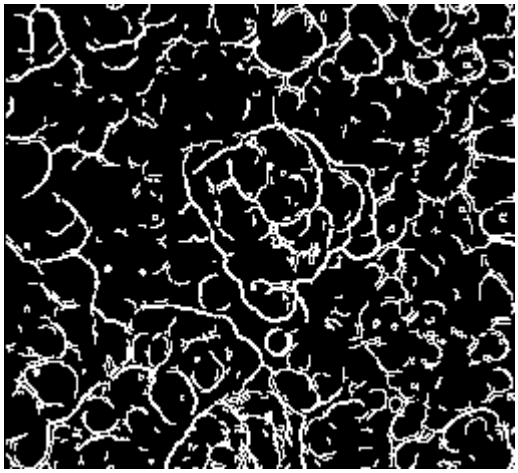
Substrate: hydroxyapatite



Substrate: composite







C.Felgueiras, J.P. Marques de Sá, 1998

Fractal modelling may help to assess the growth conditions

2 - FRACTALS IN PHYSIOLOGY

(Some Examples)

Temporal Fractals

- **Heart beat sequences**
- **Electroencephalograms**
- **Time intervals between action potentials**
- **Respiratory tidal volumes**
- **Ion channel kinetics in cell membranes**
- **Glycolysis metabolism**
- **DNA sequences mapping**

Spatial Fractals

- **Intestine and placenta linings**
- **Airways in lungs**
- **Arterial system in kidneys**
- **Ducts in lever**
- **His-Purkinje fibres in the heart**
- **Blood vessels in circulatory system**
- **Neuronal growth patterns**
- **Retinal vasculature**

- Reference: Bassingthwaighte JB, Liebovitch, L. S., West B. J. (1994) Fractal Physiology. Oxford University Press.

3 - SELF-SIMILARITY AND FRACTAL DIMENSION

Koch curve

Scale: r a.r $0 < a < 1$

Self-similarity dimension:
How many parts in an object are similar to the whole ?

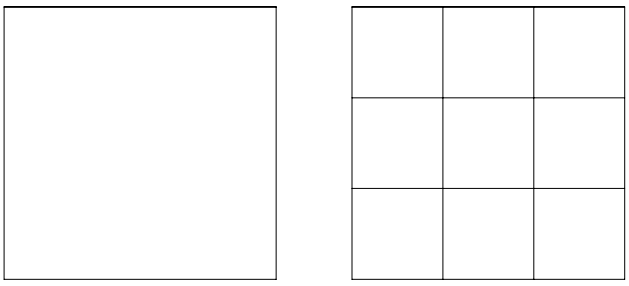
Simple Objects

Dimension = D = 1

r = 1 r = 1/3

N = 1 $N = 3 = (1/3)^{1}$

Dimension = D = 2



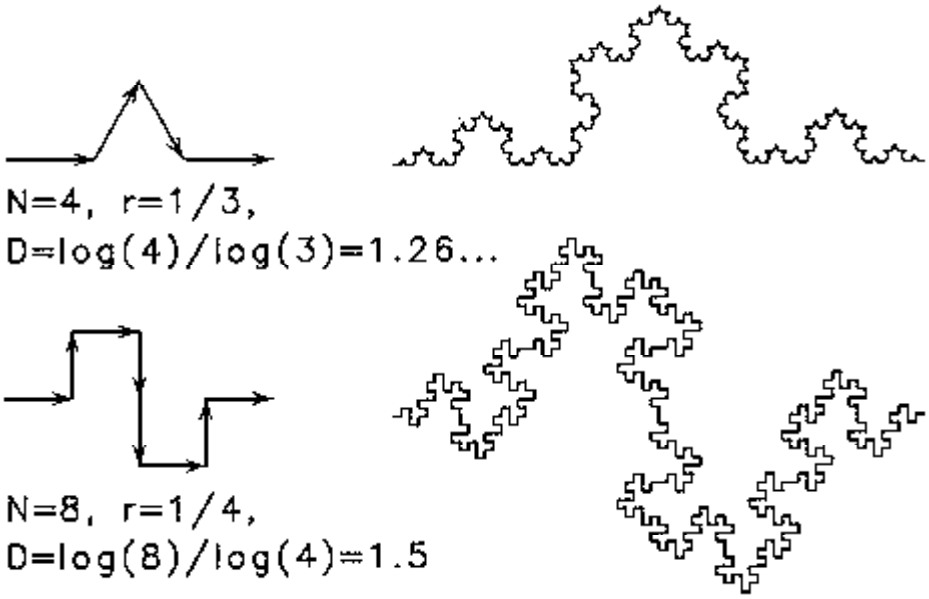
N = 1 $N = 9 = (1/3)^{2}$

Number of exact replicas N(r) when the resolution is r :

$$N(r) = \left(\frac{1}{r}\right)^{D} = r^{-D} \quad \Rightarrow \quad D = \frac{\log(N(r))}{\log(1/r)}$$

Fractal Objects

(with exact self-similarity)



Fractal:

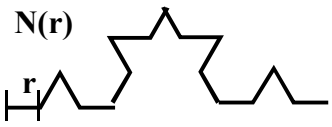
Any object with D having a fraction part?

Not always…

Any object with D > topological dimension?

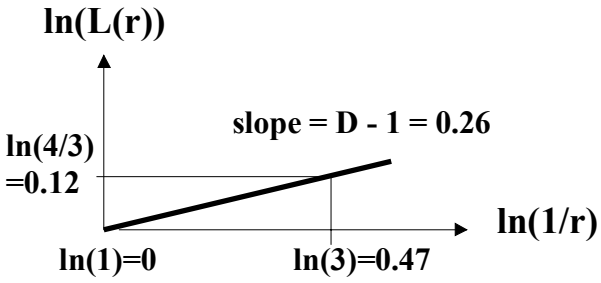
Not always…

Length of the object :



$$L(r) = r \,.\, N(r) = r^{1-D}$$

$$\ln(L(r)) = (D-1) \,.\, \ln(1/r)$$



Any object with a property L(r) satisfying a Power Law Scaling:

$$L(r) \propto r^{\alpha},$$

is said to have a fractal property L(r).

$\alpha = 1-D$	for lengths
$\alpha = 2-D$	for areas
$\alpha = 3-D$	for volumes

The scaling property can be written as:

$$L(ar) = k\,L(r) \;,$$

with $a < 1,\ k = a^{\alpha}$

and

<u>k, iteration factor, independent of r</u>

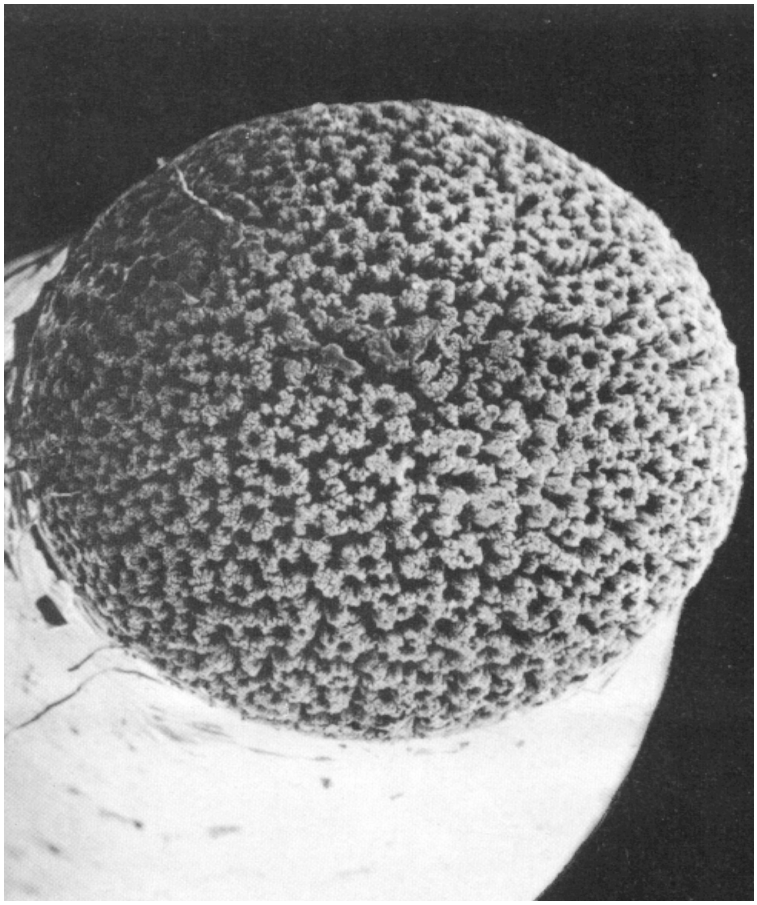
For the Koch curve:

$$r = 1 \;\Rightarrow\; L(1) = 1$$

$$r = 1/3 \;\Rightarrow\; L(1/3) = 4/3 = 4/3\,.\,L(1)$$

$$r = 1/9 \;\Rightarrow\; L(1/9) = 16/9 = 4/3\,.\,L(1/3)$$

$$L(r/3) = 4/3\,.\,L(r)$$



Cardiac Pacing Electrode

Zr – Interface impedance with roughness effect

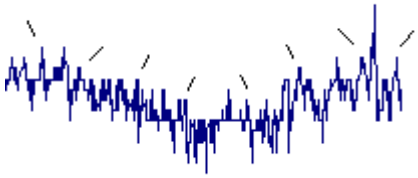
Zi – Interface impedance per unit of true interface area

$$Zr = a\,(Zi)^{\beta}$$

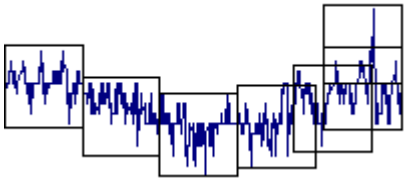
$$\beta = 1/(D-1)$$

Roughening the surface $\rightarrow$ $D \approx 3 \rightarrow \beta \approx 0.5$

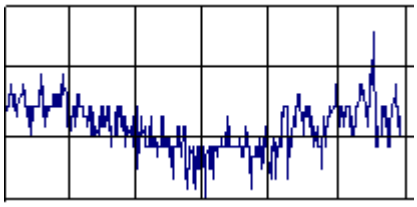
Estimating the Fractal Dimension



Length: $L(r) = rN(r) \propto r^{1-D}$



Number of covering boxes or spheres: $N(r) \propto r^{-D}$



Box-counting: number of squares containing a piece of the object

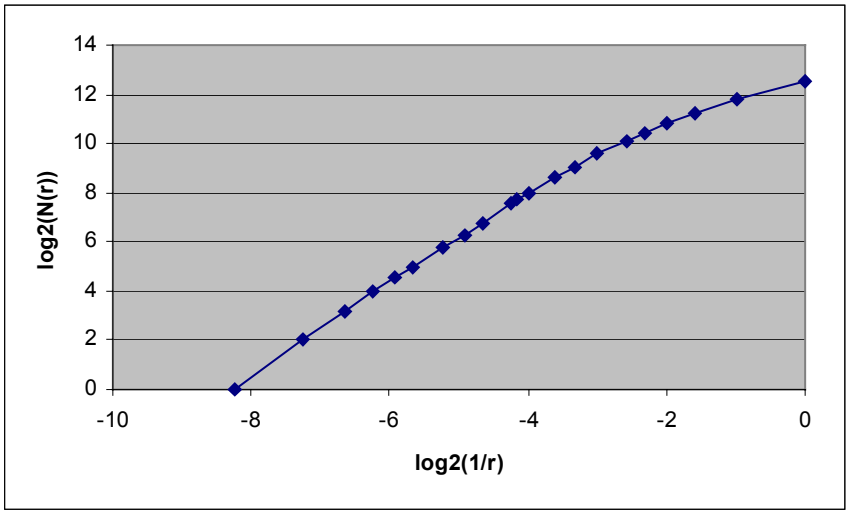
Statistical Self-Similarity

Generalisation:

$$\mathbf{D_{cap}} = \lim_{\mathbf{r} \to 0} \ln(\mathbf{N}(\mathbf{r})) / \ln(1/\mathbf{r}) \quad , \quad \textbf{capacity dimension}$$

(Grassberg and Procaccia)

Result of box-counting method applied to retina angiogram



C.Felgueiras, J.P. Marques de Sá, A.M. Mendonça (1999)

D = 1.82

Number of branching sites ∝ (cluster diameter)^{D}

Generalised Fractal Dimensions

(In a coverage of N(r) boxes of size r)

Information dimension:

$$\mathbf{D}_{\inf} = \lim_{\mathbf{r}\to 0} \mathbf{S}(\mathbf{r})/\ln(\mathbf{r}) = \lim_{\mathbf{r}\to 0} -\sum_{\mathbf{i}=1}^{\mathbf{N}(\mathbf{r})} \mathbf{p_i} \ln \mathbf{p_i} / \ln(\mathbf{r})$$

S(r) – Entropy; p_i - probability for a point to lie in box i

Correlation dimension:

$$\mathbf{D_{corr}} = \lim_{\mathbf{r}\to 0} \ln(\mathbf{C}(\mathbf{r}))/\ln(\mathbf{r}) = \lim_{\mathbf{r}\to 0} \ln \sum_{\mathbf{i}=1}^{\mathbf{N}(\mathbf{r})} \mathbf{p_i^2} / \ln(\mathbf{r})$$

C(r) : Number of pairs of points in box i

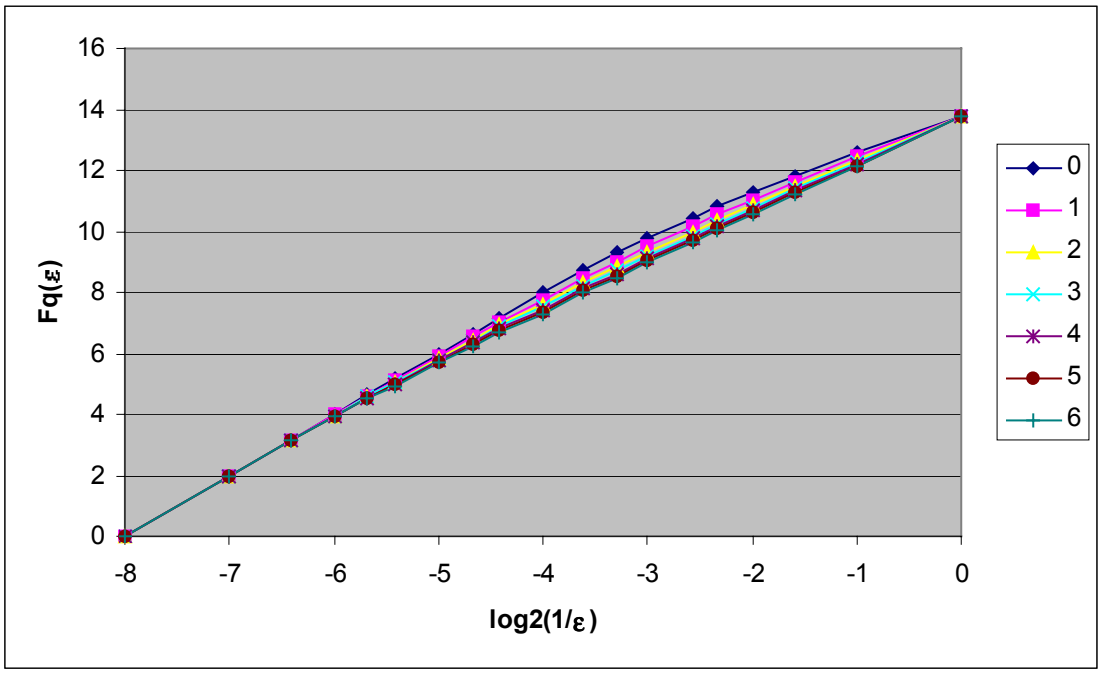
Generalised dimensions:

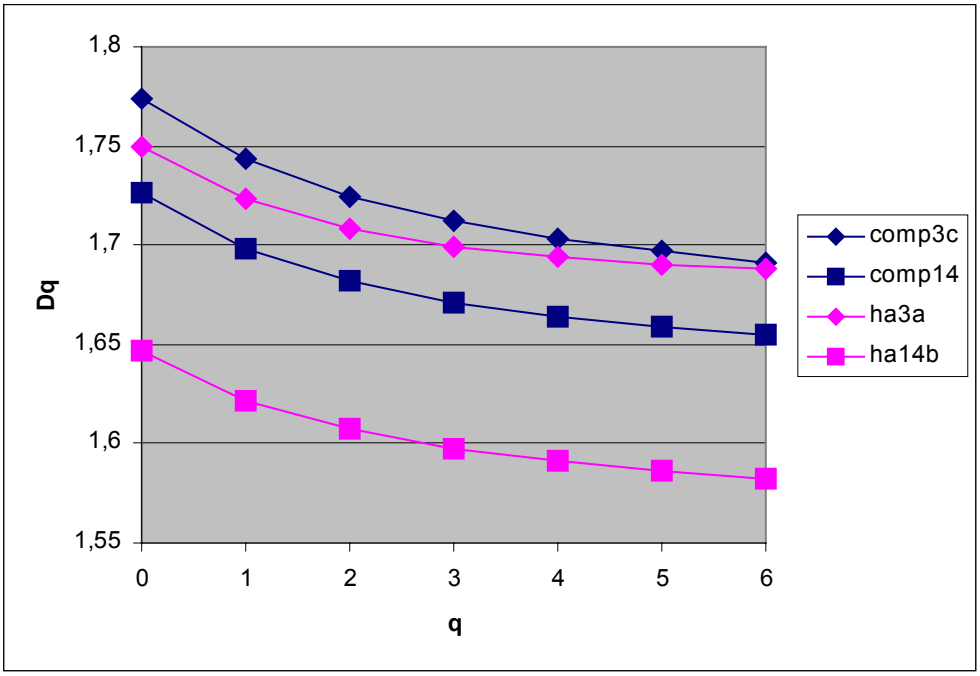
$$\mathbf{D_q} = \lim_{\mathbf{r}\to 0} \frac{1}{1-\mathbf{q}} \frac{\ln \sum_{\mathbf{i}=1}^{\mathbf{N}(\mathbf{r})} \mathbf{p_i^q}}{\ln(1/\mathbf{r})} = \lim_{\mathbf{r}\to 0} \frac{\mathbf{F_q}(\mathbf{r})}{\ln(1/\mathbf{r})}$$

$$\mathbf{D_0 = D_{cap}\ ;\ D_1 = D_{inf}\ ;\ D_2 = D_{corr}}$$

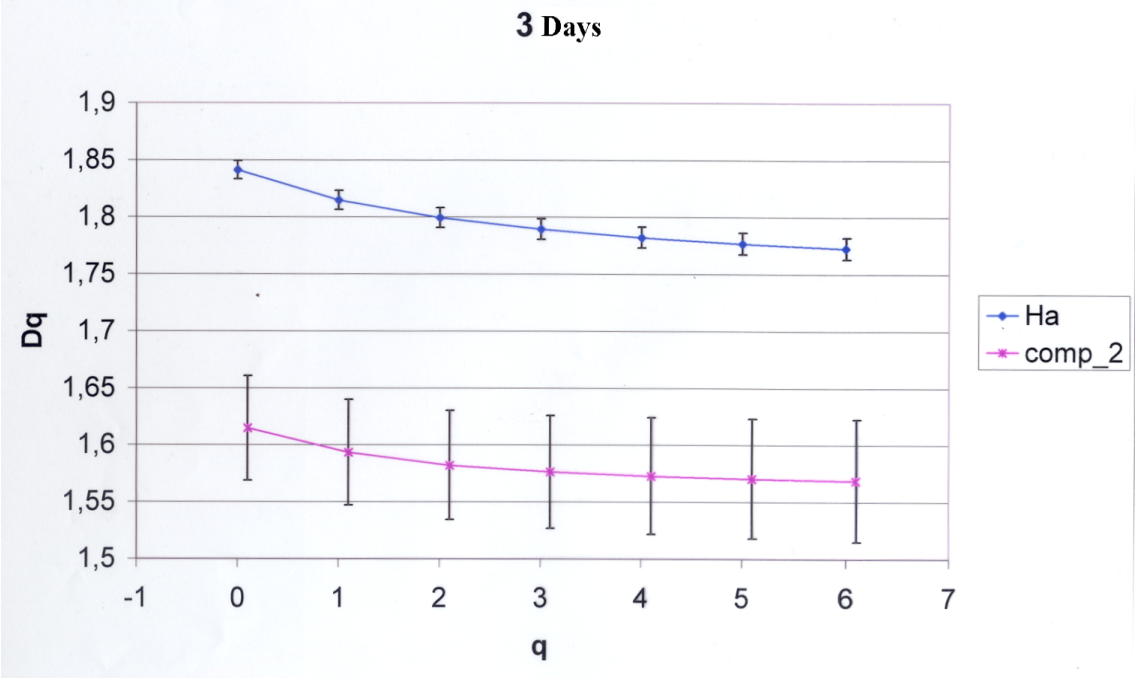
D_q decreases with q, e.g.: $\mathbf{D_{cap}} \geq \mathbf{D}_{\inf} \geq \mathbf{D_{corr}}$

Hydroxyapatite Growth on Bioactive Surfaces





ha – hydroxiapatite substrate
comp – composite glass substrate

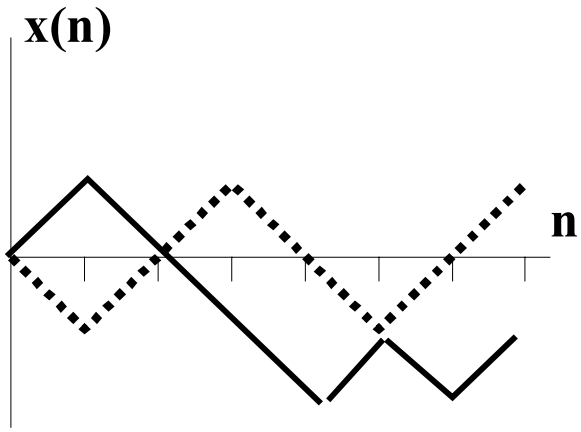


Ha – Hydroxiapatite
comp 2 – composite 2 glass

5 - SELF-AFFINITY AND THE FRACTIONAL BROWNIAN MODEL

The symmetric random walk

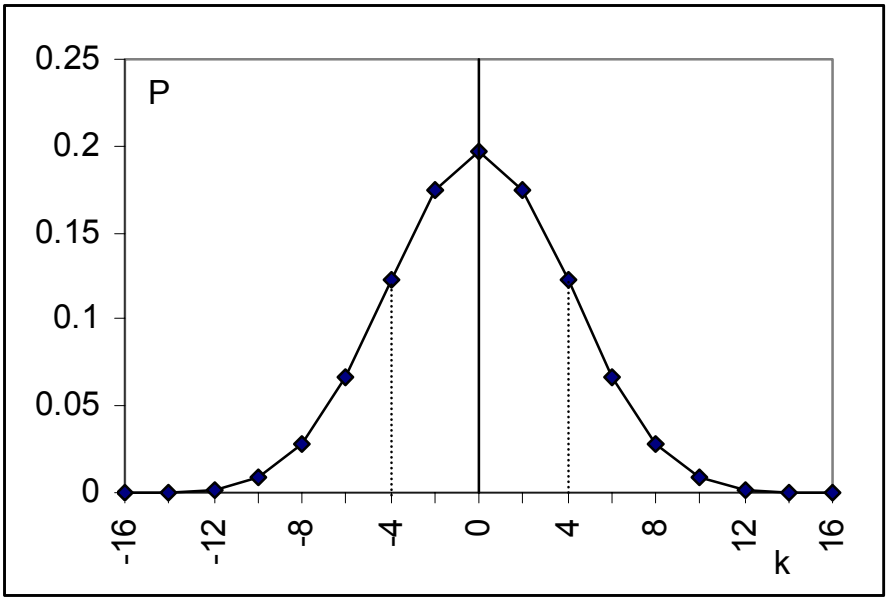
$$\mathbf{x(n)} = \sum_{\mathbf{i}=1}^{\mathbf{n}} \mathbf{x_i} \qquad ; \qquad \mathbf{P(x_i = 1) = P(x_i = -1) = \frac{1}{2}}$$



$$P(x(n) = k) = \binom{n}{\frac{n+k}{2}} \frac{1}{2^n} \qquad k = -n, -n+2, \ldots, n-2, n$$

$$\mathbf{E[x(n)] = 0} \qquad \mathbf{V[x(n)] = n}$$

Probability of the random walk for n=16.



Taking: r points per unit time
$\pm\varepsilon$ jumps

With: $r \to \infty \quad , \quad \varepsilon \to 0 \quad ; \quad r\varepsilon^2 \to \sigma^2$

Symmetric Random Walk → Brownian Motion Function

$$B(t,x) \overset{\Delta}{=} \frac{1}{\sigma\sqrt{2\pi t}} e^{-x^2/2\sigma^2 t}$$

Properties:

$B(t+\Delta t)-B(t)$:	Gaussian increments
$E[B(t+\Delta t)-B(t)]$	$= 0$
$V[B(t+\Delta t)-B(t)]$	$= \sigma^2 . \Delta t \Rightarrow \sigma[B(t+\Delta t)-B(t)] \propto \sqrt{\Delta t}$

scaling

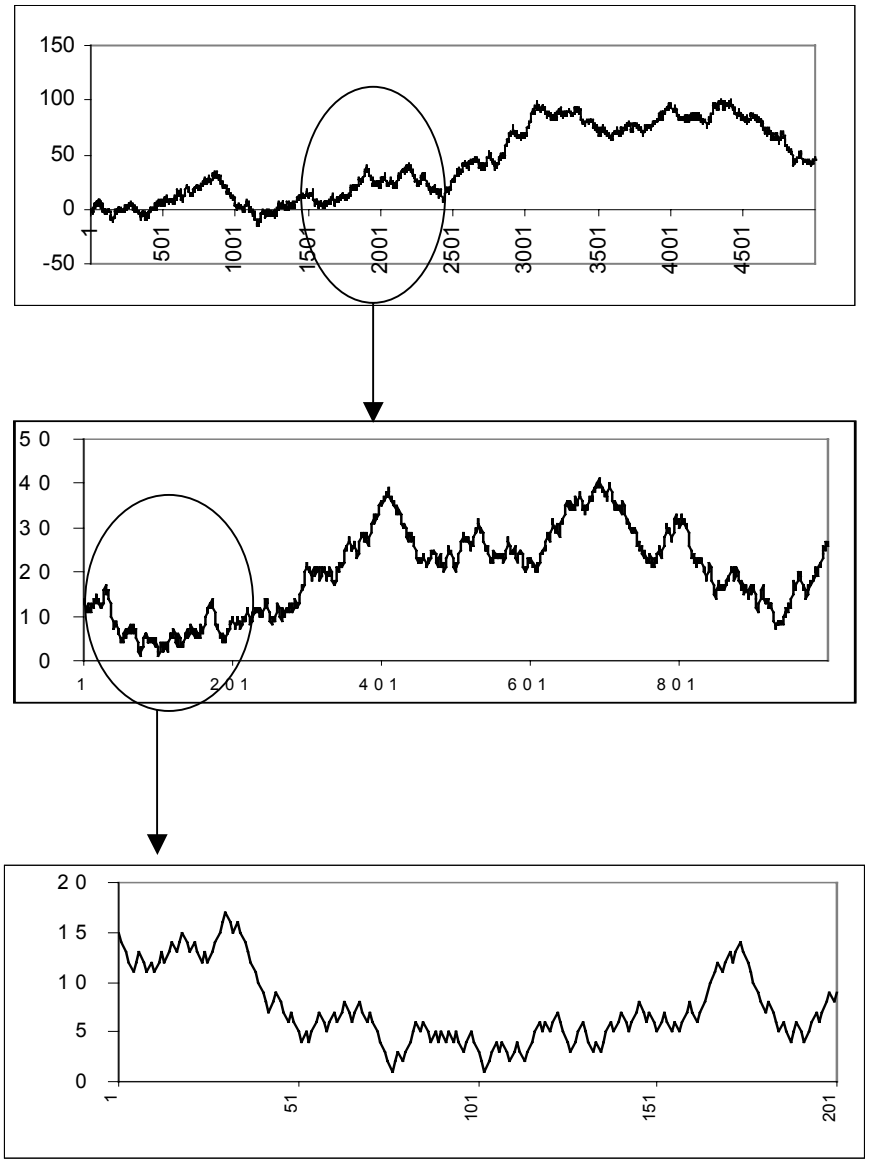
$$\sigma[B(t+\Delta t)-B(t)] \propto \sqrt{\Delta t}$$

$$\sigma[B(t+r\Delta t)-B(t)] \propto \sqrt{r\Delta t} = r^{\frac{1}{2}} . \sigma[B(t+\Delta t)-B(t)]$$

Self-Affinity

$$\Delta t \to r.\Delta t \quad ; \quad \sigma(B) \to r^{\frac{1}{2}} . \sigma(B)$$

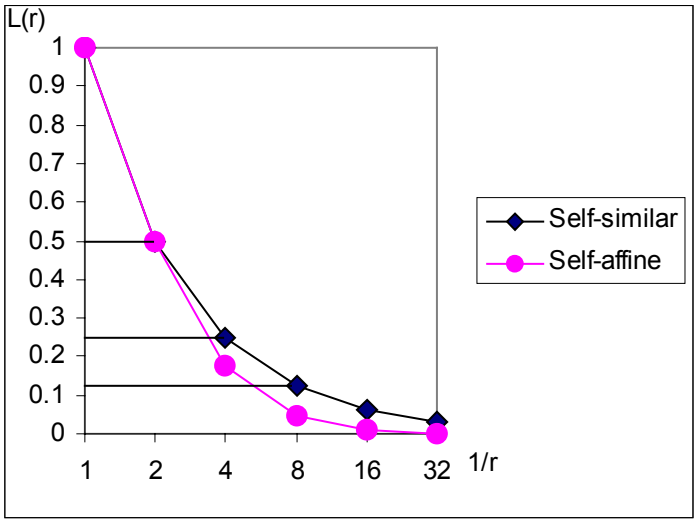
<u>Iteration factor dependent on r (compare with page 9)</u>


150
100
50
0
-50
1
501
1001
1501
2001
2501
3001
3501
4001
4501
50
40
30
20
10
0
1
201
401
601
801
20
15
10
5
0
1
51
101
151
201

Two processes:

Self-similar: $$L\left(\frac{r}{2}\right)=\frac{1}{2}L(r)$$

Self-affine: $$L\left(\frac{r}{2}\right)=\frac{\sqrt{r}}{2}L(r)$$



Fractional Brownian Motion

Def.: Moving average of B(t,x) with increments weighted by $(t-s)^{H-1/2}$ - "random walk with memory"

$$B_H(t,x) \approx \int_{-\infty}^{t} (t-s)^{H-1/2} dB(s,x) \qquad H \in]0,1[$$

Hurst coefficient

Self-affine process with : $\sigma(B_H) \propto \Delta t^H$

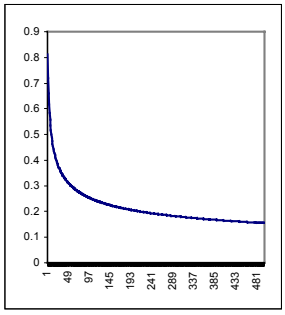
H = ½	**Brownian motion**
0 < H < ½	**fBm with anti-correlated samples**
½ < H < 1	**fBm with correlated samples**

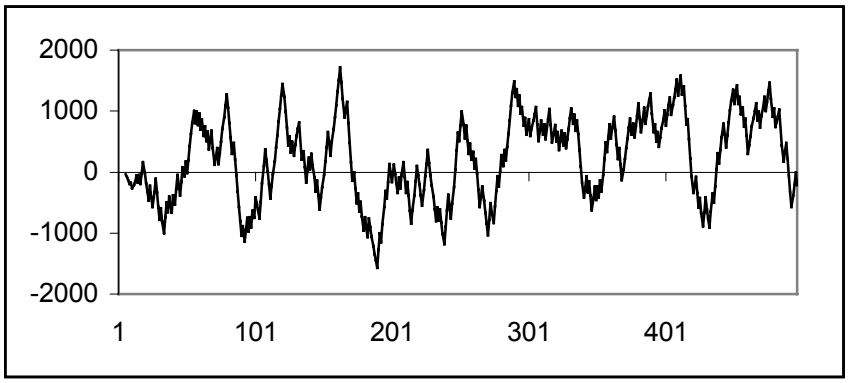
$B_H(t)$

$$\sigma(B_H) \propto t^H$$

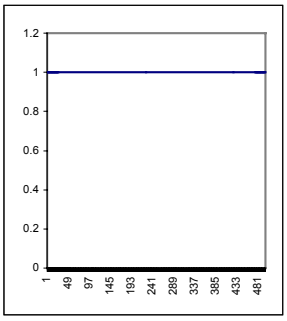
Kernel

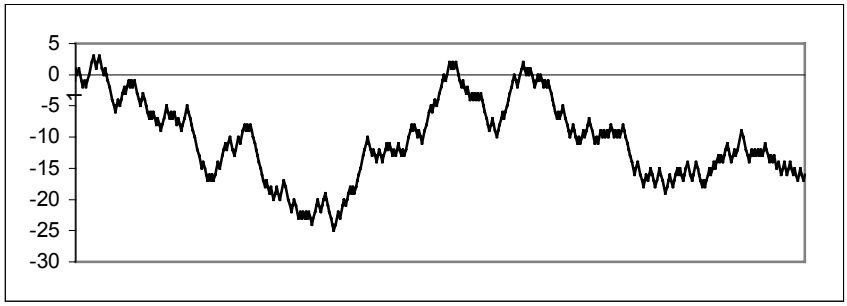
H=0.2, D=1.8



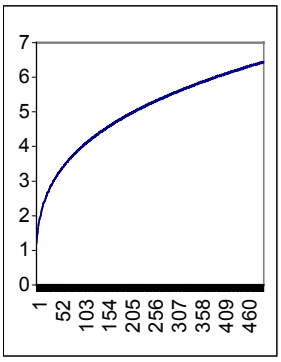


H=0.5, D=1.5

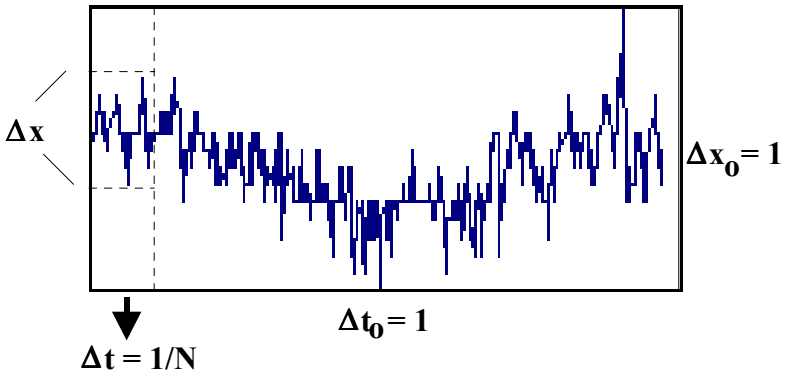




H=0.8, D=1.2



Computing the fractal dimension of the fBm :



For $\Delta t = \frac{1}{N} \quad \rightarrow \quad \Delta x = \Delta t^{H} = \left(\frac{1}{N}\right)^{H}$

The region $\Delta x \Delta t$ **is covered by:**

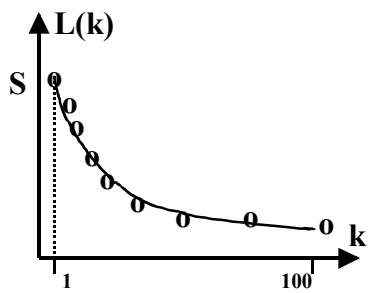
$\frac{N}{N^{H}}$ **squares of size** $L = \frac{1}{N}$

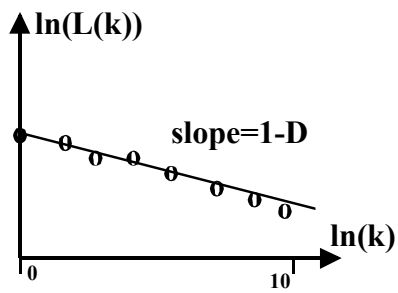
The whole segment is covered by:

$$N(L) = N.\left(\frac{N}{N^{H}}\right) = N^{2-H} = \frac{1}{L^{2-H}}$$

Therefore: $D = 2 - H$

Higushi method: $L(k)=sk^{1-D}=sk^{H-1}$





6 - Chaotic Systems and Fractality

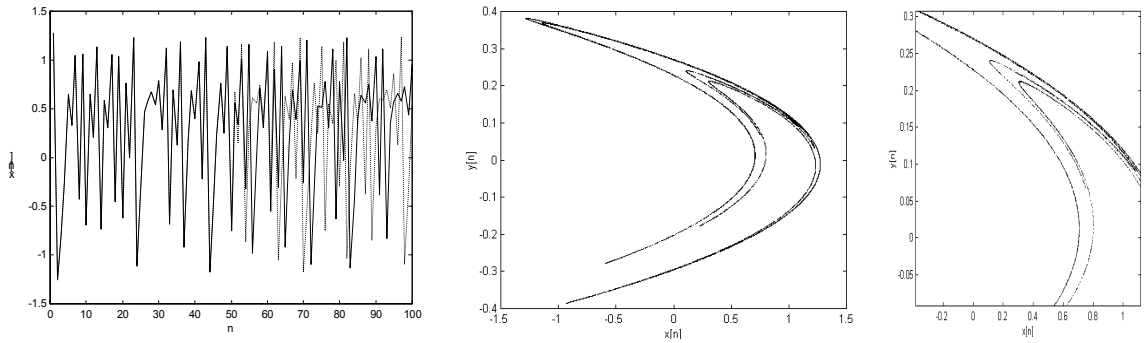
Chaotic system:

Deterministic dynamic system with high sensitivity to initial conditions.

Example:

Hénon process:

$$x(n+1) = y(n) + 1 - 1.4x(n)^2;$$
$$y(n+1) = 0.3x(n).$$



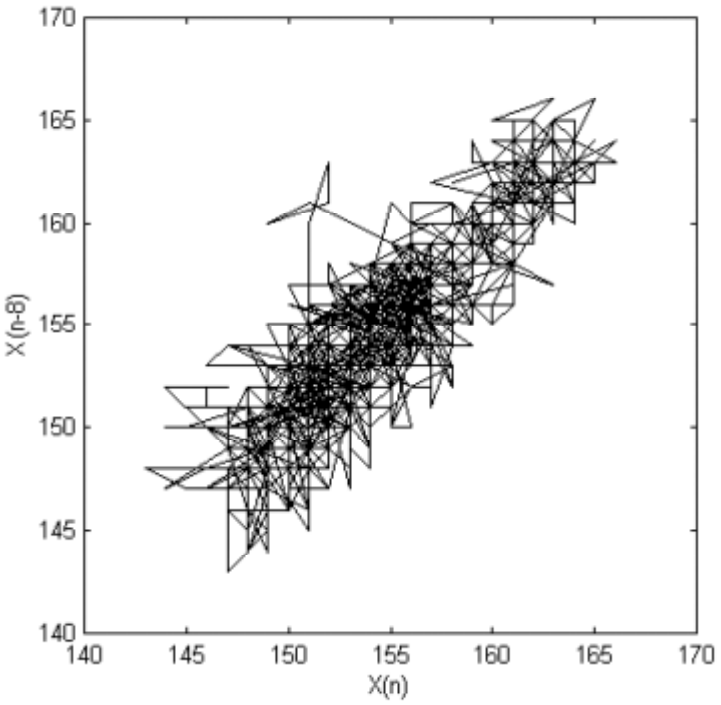
a) b) c)

Figure 9. a) Hénon process signals with initial values differing in 10^{-12}; b) Hénon attractor; c) A detail of the attractor.

Some properties:

- **High sensitivity to initial conditions.**
- **Values not predictable in the long run.**
- **System state describes intricate trajectories (attractor) in the phase space.**

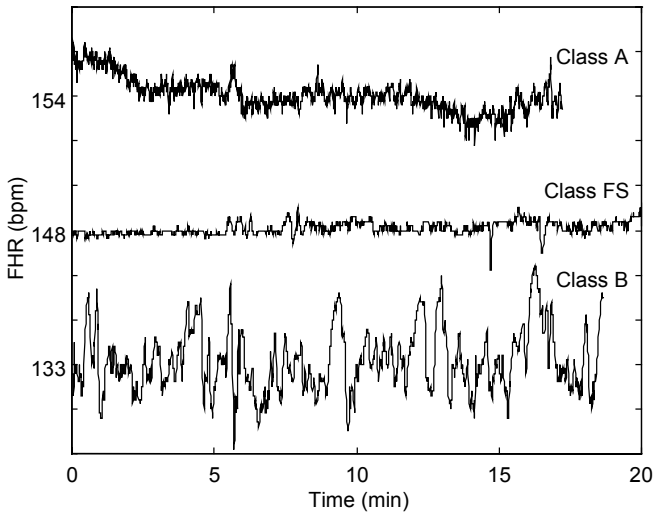
Analysis tool: Attractors in the phase-space



Takens Theorem:

The set {x[i],x[i+k],…,x[i+dk]} is topologically equivalent to the attractor in an embedding space of dimension d+1.

7 – Fractal Modelling of Foetal Heart Rate

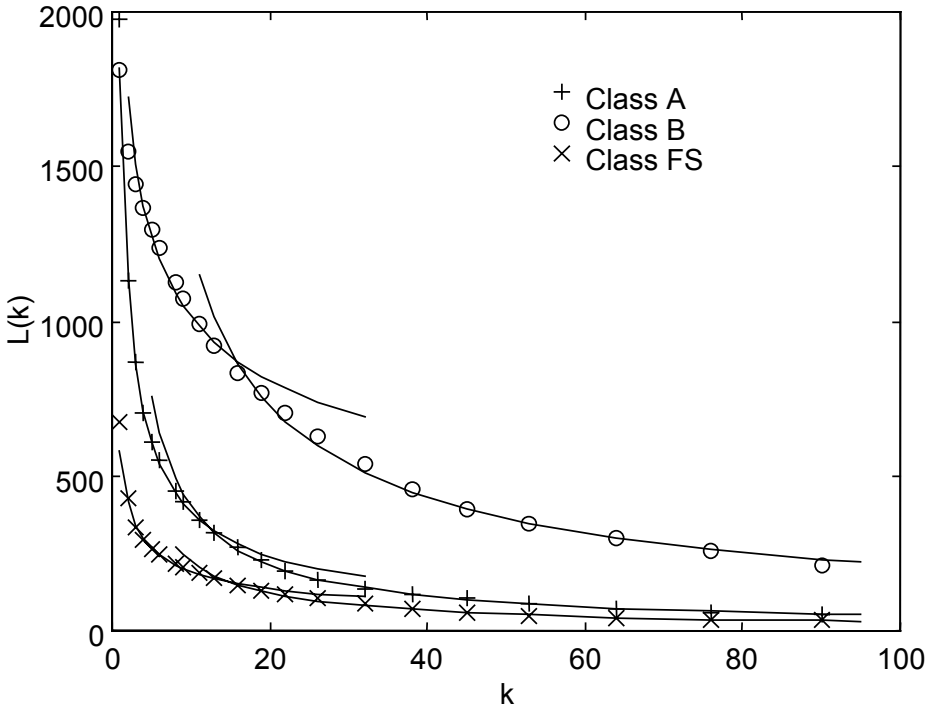


Class A – NEM sleep
31 cases

Class B – REM sleep
50 cases

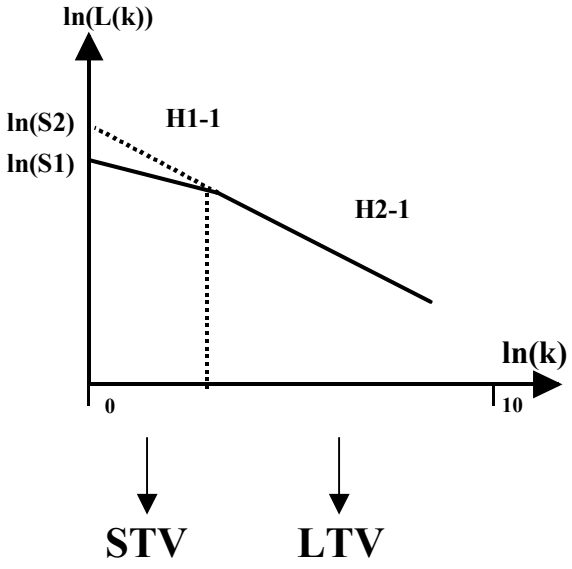
Class FS - Neuro-cardiac depression
43 cases

FHR modelling by a bi-scale fBm fractal

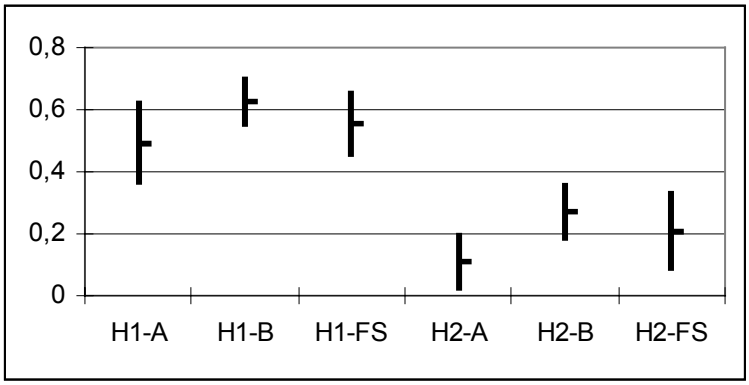


Results of Higushi method ($L(k) = Sk^{H-1}$) showing two scaling regions

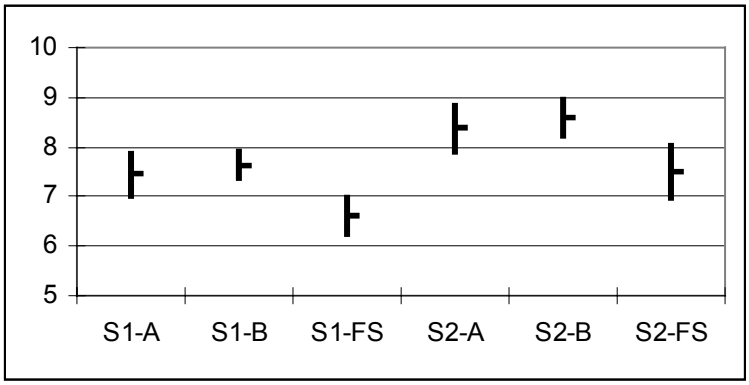
FHR bi-scale behaviour



H1, H2

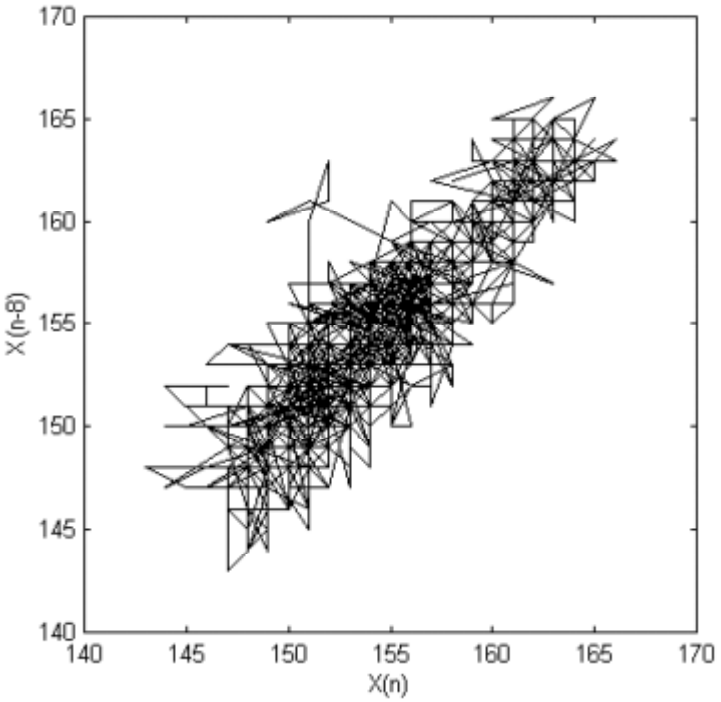


S1, S2



Foetal Heart Attractor

(Stage A; Delay= 8 samples ≈ 20 s)



C. Felgueiras, J.P. Marques de Sá (1998)

FHR Classification Results

7 Features (3 temporal; 4 attractor)

Actual Class	No. of Cases	Predicted Class A	B	FS
A	31	26 (84%)	5 (16%)	0 (0%)
B	50	2 (4%)	48 (96%)	0 (0%)
FS	43	2 (5%)	0 (0%)	41 (95%)

Training set error: 7.3% - Test set error: 15.4%

Comparison with traditional clinical method:

FHR Class	No. of Cases	*Pe %* Fractal	STV	p
A	31	16.1	67.7	< 0.001
B	50	4.0	26.0	< 0.001
FS	43	4.7	18.6	0.021
Total	124	7.3	33.9	< 0.001

C. Felgueiras, J.P. Marques de Sá, J. Bernardes, S. Gama (1998) *Classification of Foetal Heart Rate Sequences Based on Fractal Features*, Medical & Biological Eng. & Comp., 36(2): 197-201.

8 - FINAL COMMENT

Interest of Fractal Modelling in BME

- **Reveal the mechanisms that produce physiologic signals and structures.**
- **Clarify the meaning of measurements.**
- **Clarify the existence of deterministic causes in apparent random behaviour.**
- **Derive model parameters to classify data.**