Paediatric Respiratory Reviews 11 (2010) 123–131

Contents lists available at ScienceDirect

Paediatric Respiratory Reviews

Review

Fractals for physicians

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ARTICLE INFO

Keywords:
complexity
nonlinearity
detrended fluctuation analysis
power laws

SUMMARY

There is increasing interest in the study of fractals in medicine. In this review, we provide an overview of fractals, of techniques available to describe fractals in physiological data, and we propose some reasons why a physician might benefit from an understanding of fractals and fractal analysis, with an emphasis on paediatric respiratory medicine where possible. Among these reasons are the ubiquity of fractal organisation in nature and in the body, and how changes in this organisation over the lifespan provide insight into development and senescence. Fractal properties have also been shown to be altered in disease and even to predict the risk of worsening of disease. Finally, implications of a fractal organisation include robustness to errors during development, ability to adapt to surroundings, and the restoration of such organisation as targets for intervention and treatment.

WHY SHOULD A PHYSICIAN CARE ABOUT FRACTALS?

"Nothing in Nature is random. ... A thing appears random only through the incompleteness of our knowledge."
Baruch Spinoza

Physicians may find themselves increasingly coming across the terms "fractals", "nonlinear dynamics" and "complexity" in the medical sciences literature. At the time of writing, a search on "fractals" alone on Pubmed yielded 2063 articles. This number is expected to grow rapidly. There is a journal dedicated to the topic of fractals in medicine and biology.

Behind this enthusiasm is the idea that living systems are not the simple, single-compartment or linear processes we often assume them to be, nor are they usually random in behaviour. Thus, more complex methods are required to characterise them and the output signals they generate. By studying them over a narrow range of linear behaviour fitting our assumptions, or by simply looking at averaged values of their output, we neglect information such as the dynamic properties of the system, i.e. how the system changes over time.

Fractal analyses constitute a subset of these complex methods. In the next few sections, we provide an overview of fractals, of techniques available to describe fractals in data, and we propose some reasons why a physician might benefit from an understanding of fractals and fractal analysis. A number of excellent past reviews have been written about fractals or complexity for a medical,[1,2] physiological[3] and even epidemiological[4] audience, including a glossary to clarify some of the jargon present in the medical literature on this topic.[5] Thus, this review will attempt to include more recent findings, and where possible will additionally focus on the respiratory system, particularly in paediatrics.

FRACTALS ARE EVERYWHERE

"Why is geometry often described as 'cold' and 'dry?' One reason lies in its inability to describe the shape of a cloud, a mountain, coastline, or a tree. Clouds are not spheres; mountains are not cones, coastlines are not circles, and bark is not smooth, nor does lightning travel in a straight line."
Benoit Mandelbrot[6]

What are fractals?

Examples of fractals abound in nature, from clouds, trees, mountain ranges, snowflakes, to the branching pattern of rivers (Figure 1). Mandelbrot was the first to account for the complexity of the systems found in the body with the concept of fractals.[6] He defined a fractal as an object with *self-similar* organisation, i.e. details of the structure at smaller scales have a similar form to the whole (Figure 2). Furthermore, a fractal is not smooth and homogenous in form, and when examined at greater levels of magnification, progressively greater details of the structure are observed (*scaling*), and there exists no characteristic scale with which to describe the structure (*scale-invariance*). Self-similar structures obey a nonlinear, *power law* relation, where some

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doi:10.1016/j.prrv.2010.02.001

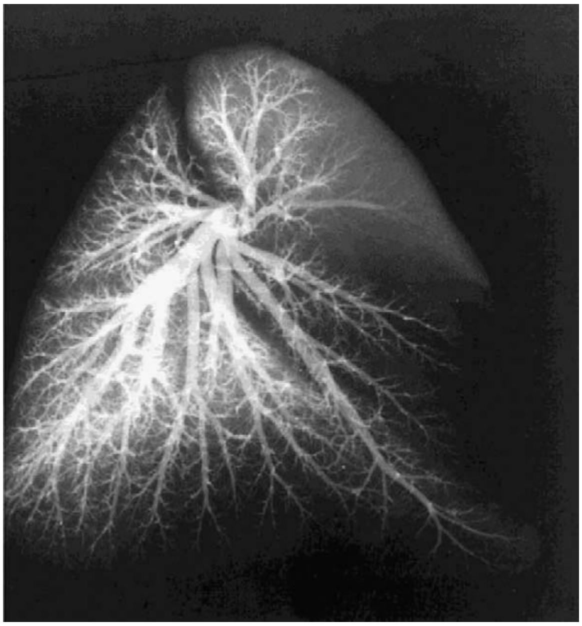

Figure 1. An example of a fractal structure – the pulmonary vascular tree in a human infant (used with permission[44]).

physical measure of the structure *L(r)* is related to the scale at which it is measured *r* via a power or scaling exponent α:

$$L(r) = A\,r^{\alpha} \tag{1}$$

where *A* is a constant.

Fractals in time

The concept of fractals can be applied not only to structural forms that lack a single characteristic length scale, but also to signals that lack a single characteristic time scale. Here, the relationship between the statistical properties of the fluctuations in the signal and the time window of observation is scale-invariant or follows a power law (Figure 2). One corollary of this behaviour is that future values in the signal are dependent on the past, i.e. the signal displays *correlations* over time, and the system producing the signal can be said to exhibit *memory*. That the future behaviour of the system is a consequence of past behaviour is described as *determinism*. Fluctuations in weather patterns, pollutant levels, ocean temperatures, and even the stock exchange may appear random, but all have been found to exhibit statistical self-similarity. Fractals in biology are not necessarily scale-invariant over all scales, but rather exhibit self-similarity over a finite scale.

How can we quantify fractals?

We present here a few methods to quantify fractals in space and time which are frequently encountered in the medical literature. The list is by no means comprehensive, and the interested reader is referred to other sources[3,7] for additional techniques.

The *fractal dimension* describes the extent to which an object fills the space available over different scales. Whereas the fractal dimension of geometric objects would be an integer, for a fractal object it is a non-integer or fractional value (hence the term fractal). For example, a straight line has a fractal (and geometric) dimension of 1, a curve has a dimension of 2, and a fractal "line" will have a fractal dimension between 1 and 2. Correspondingly, a fractal surface will occupy a fractal dimension between 2 and 3. The fractal dimension is in essence also a measure of "irregularity"

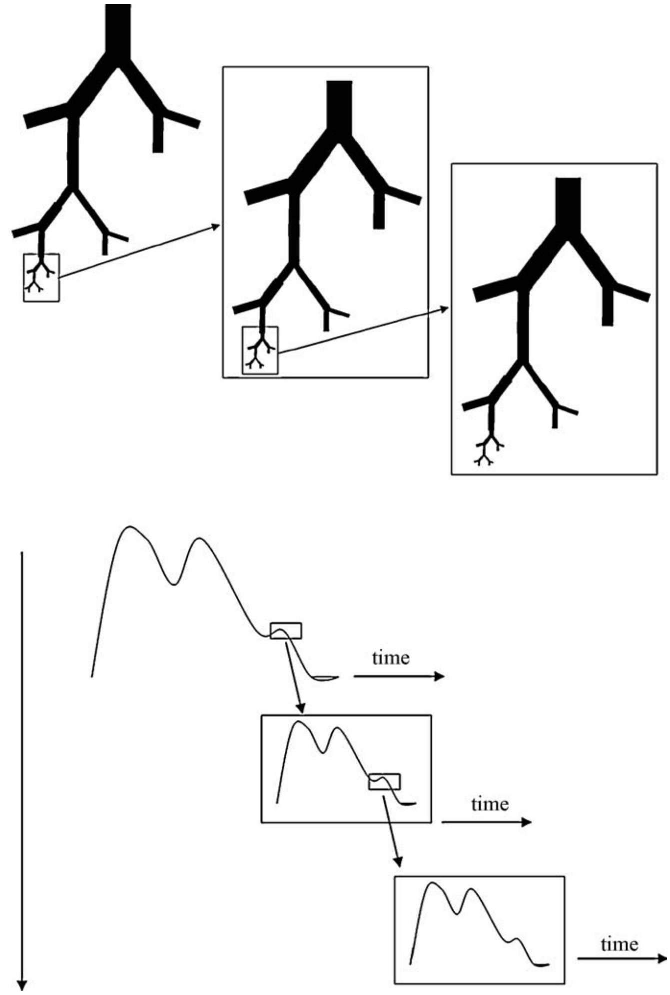

Figure 2. Ilustration of a fractal structure over length scales (top panel) and a statistically fractal signal over time scales (bottom panel). Details of the structure or signal at smaller scales have a similar form to the whole, and when examined at greater levels of magnification, progressively greater details of the structure or signal are observed. With a fractal structure, a geometric quantity such as length or area is measured, whereas with a fractal signal, some statistical quantity of interest is measured (Adapted from Frey and Suki, 2009 with permission[62]).

– a highly irregular line filling up two-dimensional space would have a higher dimension closer to 2, in contrast to a smoother line which would have a lower dimension closer to 1. Calculation of the fractal dimension can be conceptualised as using a ruler to measure the contour length of a structure.[3] As the length of the ruler decreases and finer details of the structure are revealed, the measured length of the structure increases. In a fractal object, the measured length of the structure *L(r)* will be related to the length of the ruler *r* via a power law of the form of Equation (1), and the fractal dimension is the scaling exponent α. In practice, the power law relationship is plotted in a log-log manner so that a linear graph is obtained, and α is given by the slope of the line of best fit.

Most methods to quantify fractal signals in time are analogous to the fractal dimension, but applied to the time rather than length scale, and using some statistical measure of the signal fluctuations about the mean instead of the measured length. In *Hurst rescaled range analysis*,[3,7] the statistical measure of interest is the local range of the signal divided by the standard deviation over an observation time window. This measure generally increases with the length of the time window following a power law, with an exponent denoted H ranging from 0 to 1. A higher H implies increased correlations in time. Hurst analysis has conventionally