Fractals in Clinical Hemodynamics

IN this issue of ANESTHESIOLOGY, Bishop *et al.* report on a novel approach to the interpretation of hemodynamic analysis, namely fractal and multifractal.[1] Although the readers of this journal are intimately familiar with the cardiovascular system and its gyrations in response to stress, surgery, and anesthetics, the application of fractals and specifically of multifractals to data synthesis and interpretation initially might seem beyond the reach of, or relevance to, practitioners. My purpose in writing this commentary is to offer context and perspective to what the authors have done and what it might mean to today's clinician, and to tomorrow's.

"… multifractal variable physiology … is not only a signature of health but also a potential therapeutic tool …"

First, let us observe that those of us who care for sick patients in highly technical environments are data-rich and information-poor. We who care for sick patients—whether in the operating room on in the intensive care unit—cannot possibly accumulate, absorb, and synthesize the streaming waveforms or their 6-s scalar snapshots (the glowing digits that announce a heart rate to be 82 beats/min, a blood pressure to be 116/54 mmHg, and so on) that dance across the monitor. Interpretive strategies abound, the simplest of which is to create a time series of values and then attempt to give some statistics on the time series. Technological considerations aside, modern hardware and software make it easy to determine the time intervals between heartbeats (or its reciprocal, the instantaneous heart rate), the series of systolic and diastolic blood pressures, and so forth.

Anesthesiologists are rightly most concerned about gross trends: the heart rate going up and the blood pressures going down signals a problem with intravascular volume, the blood pressure going up and the heart rate going down suggests an intracranial catastrophe, and so forth. But what if there is no apparent trend? What if the values are seemingly scattered around some value we call "normal"? Isn't this just "regular rate and rhythm"?

It is not. Normal hemodynamics (and several other aspects of physiology) are inherently—if subtly—variable.[2] Moreover, changes in the character of that variability often herald substantial changes in patient condition.[3] Therefore, it is a matter of some interest to characterize that variability and more importantly to detect and describe those changes before gross deterioration of the patient.[4]

The general structure of hemodynamic time-series variability is fractal. Like branching from a tree-trunk (each branching level produces more, but smaller, branches), the variability of physiology is characterized by coarser and finer excursions. Conventional measures of dispersion do not do us much good in talking about instantaneous heart rates, any more than they help us pick out a good-looking tree at the horticultural center. The key point is that the variability of health physiology can be analyzed on different temporal scales. One way to go about assessing variation across scales of time is to "coarse-grain" the data, that is to average adjacent data points (pairs, threes, fours, described as scale 2, scale 3, scale 4, and so forth) and reassess the variability at scale. This is a basis for multifractal assessment.[5] The analysis of data from *chronic* illnesses (such as congestive heart failure) produces very different patterns across scales, typically reflecting loss of variability. Moreover, such analyses seem to predict important clinical outcomes.[6]

All of this is prelude to the work presented in this issue of ANESTHESIOLOGY. Bishop *et al.* reasoned that the stress of operation and the interventions of the anesthesiologist might *acutely* alter the mechanisms that give rise to multifractality in human physiology. They acquired the available signals—electrocardiograph and continuous blood pressure—and processed those signals into beat-to-beat time series. Next, they used wavelets to identify how much fractality was present in the time series at different points in care.

Why wavelets? It's easiest to ask why not a Fourier transformation. Recall that any time series (or for that matter, any polynomial) can be represented as a sum of sine waves of different frequencies. That is the Fourier transformation. We "hear" the Fourier transform every time we play music on an

Photograph: J. P. Rathmell.

Accepted for publication July 11, 2011. The author is not supported by, nor maintains any financial interest in, any commercial activity that may be associated with the topic of this article.

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◆ This Editorial View accompanies the following article: Bishop SM, Yarham SI, Navapurkar VU, Menon DK, Ercole A: Multifractal analysis of hemodynamic behavior: Intraoperative instability and its pharmacologic manipulation. ANESTHESIOLOGY 2012; 117:810–21.

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MP3 player—the digital bits that we download are no more than the coefficients that set the strengths of different tones (sine waves) that are combined to hear our favorite tune.

Wavelets accomplish much the same thing, with an important exception. Fourier coefficients localize frequency across an entire time series, but wavelets localize their information in both frequency and time and thus can encode *localized variability within the time series*. Of course, just encoding the variability is not enough, one has to have a standard way of finding and describing that localized variability. That way is the tongue-twisting "wavelet modulus maxima technique" used by the authors. It turns out that just knowing the "wavelet modulus maxima" is enough to almost completely reconstruct a time series. It also enables one to characterize how much "multifractality" there is in a time series through display of a "singularity spectrum." The "singularities" that are being characterized are the steps (slow excursions) and cusps (rapid excursions) in the time series.

A singularity spectrum typically looks like a parabola. It has a maximum (the peak) and a spread (a convenient way of describing the spread of a parabola is to describe its width at half height). Where that maximum occurs characterizes the dominant fractal dimension. The width at half height gives a sense of multifractality (fig. 1 in article by Bishop *et al.*).

Evidence continues to accumulate that variable physiology, especially multifractal variable physiology, is not only a signature of health but also a potential therapeutic tool when applied *via* a physiologic support device, such as a mechanical ventilator or cardiopulmonary bypass device.[7–9] Novel ventilator modes, such as adaptive servo ventilation, demonstrate that application of variable support in one physiologic system (respiratory system) promotes variable physiology in a linked system (cardiac).[10]

What can we conclude from the article by Bishop *et al.*, which shows us that a vasoconstrictor alters the fractal dimension of the blood pressure (but not the heart rate) while atropine alters the fractal dimension of the heart rate (but not the blood pressure)? What can we conclude from the failure to detect a change in multifractality with either agent? Simply that acute management of anesthetized and critically ill patients alters the physiologic regulatory mechanisms in ways that cannot otherwise be detected with conventional displays. As the authors freely acknowledge, this is a pilot study, and much remains to be done. As readers, and more importantly as clinicians, we should understand that hidden within the rivers of data marching across the monitors is additional information about the compensatory mechanisms that drive patient physiology and our care. Fractal analysis of physiologic data is not yet ready for use at the bedside. But it is coming in our clinical lifetimes.

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