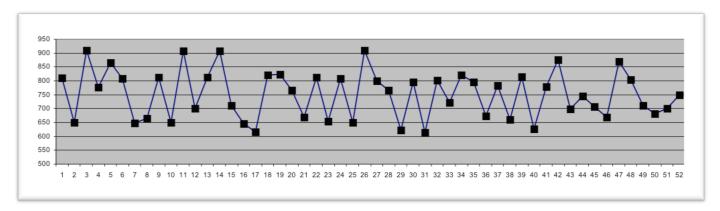
## A BRIEF DISCUSSION OF MULTISCALE ENTROPY

The process known as multi-scale entropy detects a specific kind of pattern in ordered sequences of data.



**Figure 1.** The figure above shows a series of 52 data points representing, e.g., milliseconds between consecutive heartbeats. Thus the first point represents an 805ms interval between the first and second heartbeats; the second data point represents 646ms between the second and third heartbeats, and so on.

Multiscale entropy analysis combines two separate mathematical processes known as sampled entropy and scale factoring. To begin calculating the sampled entropy, the process identifies all instances in the series where the values of two adjacent data points correspond closely (and in the same order) to the values of the *first two* data points.<sup>1</sup> Put another way, the program identifies all instances where the specific "two-in-a-row" *pattern* of the first two points is repeated. In the figures here, this pattern occurs wherever a value close to 805ms is immediately followed by a value close to 646ms, seen in figure 2 below as a green-point-followed-by-red-point pattern.

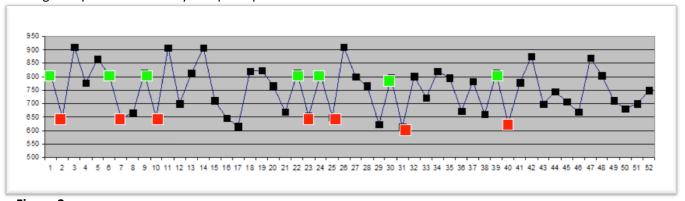


Figure 2

In the next step of determining sampled entropy, patterns closely corresponding to the three-in-a-row pattern of the first *three* data points are identified, shown in figure 3 below as the green-red-blue sequences. It will be obvious, upon reflection, that each of these matching 3-point groups must of necessity have "begun as" one of the matching 2-point patterns in the previous step. Next, the process

<sup>&</sup>lt;sup>1</sup> The user determines how far above or below one value a subsequent one can fall and still be considered to "match" the first. This range is commonly chosen as 10%-20% of the standard deviation for the whole series.

calculates the proportion of all instances where a matching 2-point sequence "turns into" a matching 3point sequence.

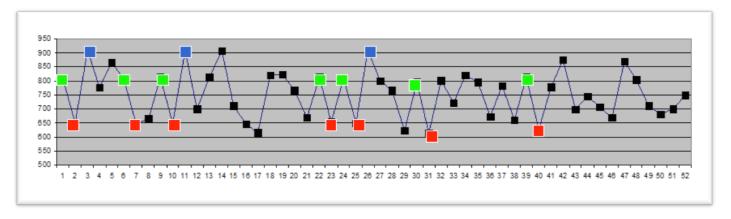


Figure 3.

Next, the entire process is repeated with a "frame-shift" of one data point. In other words, the program calculates the proportions of instances where the specific two-in-a-row pattern of the second and third data points (here, the new green-followed-by-red pattern) "turns into" the specific three-in-a-row sequence of the second, third, and fourth data points. This process continues repeating with an additional frame-shift of one data point each time, and when eventually complete for the whole series, the ratio of the total number of 2-point matches divided by the total number of 3-point matches is the basis for the sampled entropy. The sampled entropy thus "reflects the probability that sequences that match each other for the first two data points will also match for the next point", see figure 4 below (Costa 2005 at 021906-4).

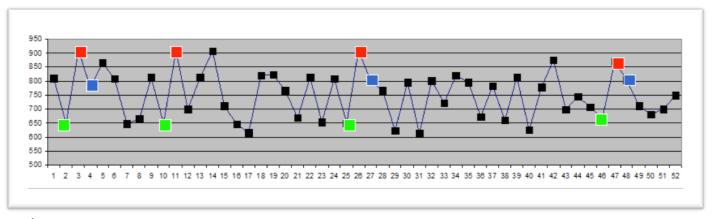


Figure 4.

<sup>&</sup>lt;sup>2</sup> Specifically, sampled entropy is the natural logarithm of this ratio.

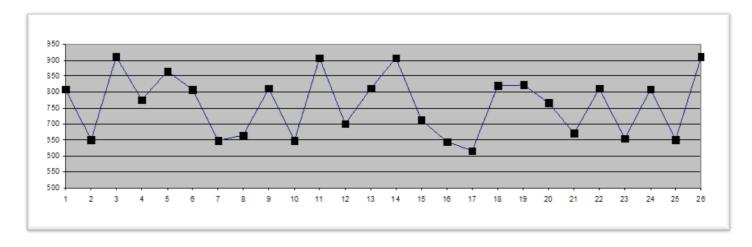


Figure 5.

Applying scale factor analysis to a series of data points involves repeatedly dividing the whole sequence into increasingly long groupings of consecutive data points, taking the average of each sub-group, and making a new sequence consisting of those values. For example, using the same series of data points as in Figure 1, applying a scale factor of 2 divides the original sequence into groups of two which are then averaged, resulting in a new sequence whose data point #1 will be an average of the values of original data points 1 and 2; new data point #2 is an average of the values of original points #3 and #4, and so on. Thus for a scale factor of 2, the resulting sequence will contain exactly half as many total points and will have a new (but related) pattern, as shown above in figure 5.

This new sequence of points resulting from applying a scale factor of 2 can now be subjected to its own sampled entropy analysis in the same way as the original series was.

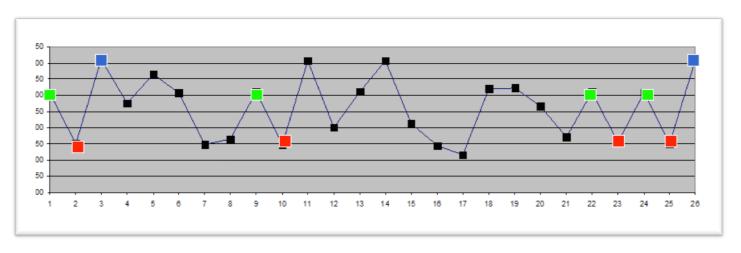


Figure 6

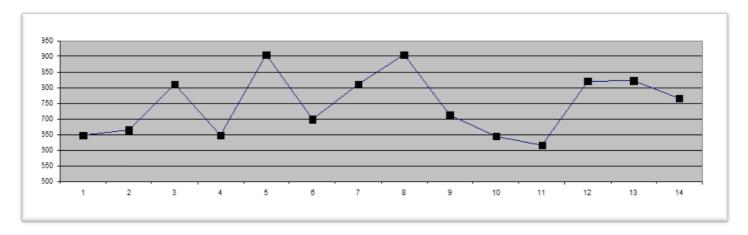
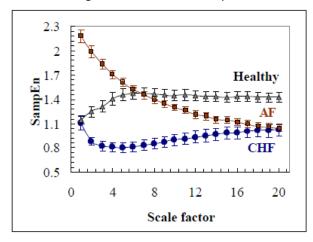


Figure 7

For scale factor of 3, new point #1 is the average of the values of original points 1-3, new point #2 is the average of original points 4-6, new point#3 is the average of points 7-9, etc., producing yet another distinct series which will then be subjected to its own distinct sampled entropy analysis.

When the sampled entropy has been calculated at each scale factor from 1 through an upper limit chosen by the researcher, a plot is then constructed with sampled entropy on the y-axis and scale factor on the x-axis. The multiscale entropy of a data sequence refers to this relationship of sampled entropy as it varies across a range of scale factors, adapted from Costa 2005.



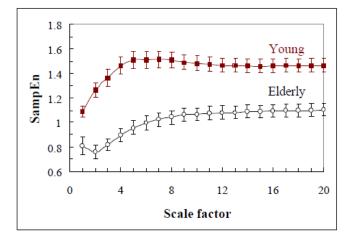


Figure 8

It is crucial to understand that these x- and y-axes represent entirely different [things] than the axes in the previous graphs. Here, *each* dot on the graph represents the culmination of the mathematical process described in the figures above; the y-axis reflects the increasing size of the individual "chunks" that the whole series gets broken into as described above. Time is not represented at all on graphs of MSE. The length of time represented on the original y-axes is subsumed into each point by the sampled entropy calculation process.

The complexity revealed by MSE is a unique species of pattern for which, unfortunately, no satisfactory vocabulary exists. Mathematicians use terms like "richness of complexity" to describe this trait, although there is no consensus on the precise meaning, apart from a general agreement that in biological processes like HRV more complexity reflects greater adaptability and health. Moreover, the word "complexity" in this setting is a bio-mathematical term of art whose precise meaning differs from its colloquial meaning in subtle but important ways. For example, most intelligent and informed laymen would probably consider the irregular heart rate pattern of atrial fibrillation as "more complex" than a steady sinus rhythm, whereas bio-mathematicians would not. A useful concept may be to think of the complexity measured by MSE as a kind of dynamic balance between pure randomness and complete regularity, each of which is antithetical to MSE's particular richness of complexity.<sup>3</sup>



The figure above illustrates this point by showing the observed MSE plots for a set of wholly random data (such as white noise or HRV in atrial fibrillation) and a set of wholly regular data (such as the intervals between beats of a metronome). The plot of the perfectly regular beats of a metronome will yield an initial sampled entropy of zero<sup>4</sup> and it will remain zero across all scale factors; since all values in the sequence will be the same, averaging increasingly large subsets will not affect anything. Similarly, the complete absence of any underlying pattern in white noise becomes more apparent as the scale factors increase, and the sampled entropy quickly approaches zero. <sup>5</sup>

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<sup>&</sup>lt;sup>3</sup> CF Costa 2005 at page 1: "There is no straightforward correspondence, however, between regularity and complexity. Neither completely predictable (e.g., periodic) signals, which have minimum entropy, nor completely unpredictable (e.g., uncorrelated random) signals, which have maximum entropy, are truly complex, since they can be described very compactly. There is no consensus definition of complexity. Intuitively, complexity is associated with 'meaningful structural richness' incorporating correlations over multiple spatiotemporal scales." (references omitted)

<sup>&</sup>lt;sup>4</sup> Since all values in the plot are exactly the same, the ratio described above in Figs. 2 and 3 will be 1. The sampled entropy will be the natural logarithm of 1, which equals 0.

<sup>&</sup>lt;sup>5</sup> As the size of a group of entirely random numbers increases, the average for that group tends to become closer to the halfway point between the upper and lower limits of the range (e.g., the average of 30 ordinary dice all rolled at once will likely be much closer to exactly 3 than will the average of 2 rolls), and their plot thus looks more and more like a straight horizontal line. As this happens, the groups of two- and three-in-a row (see Figs. 1-3 above) on that plot each grow to look more and more like 3 points in a straight line, and thus more and more like *each other*. As a result, the ratio described in Figs. 2 and 3 approaches a value of 1, and its natural logarithm approaches 0.

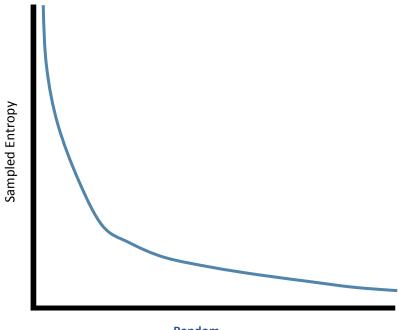


Figure 9 Random

As mentioned above, it is generally agreed that in most settings greater complexity reflects greater health. The importance of MSE as a new tool for investigating biological systems rests on its ability to reveal complexity that is undetectable by other methods.