Yang *et al.* Reply: The preceding Comment [1] on our recent Letter [2] states that (1) our dissimilarity index does not fulfill essential properties of a distance metric and (2) use of conventional statistics based on heart rate mean and variance are sufficient to obtain the "essential" results. While we concur with the first comment, the second point is misleading and needs to be addressed.

First, the proposed dissimilarity index was not intended to be a mathematically rigorous distance measure. This point is clearly evidenced by our italicized use of the term *similarity* and the quotation marks enclosing the term "distance" when the similarity measurement is first introduced in [2]. This distinction was discussed more explicitly in a subsequent longer article [3] where categorization based on the same concept of a dissimilarity index was applied in a different context (literary text analysis). We regret any inadvertent confusion created by our wording and welcome the clarification of [1].

The key question posed in the second point of [1] is whether the proposed dissimilarity index can "be useful as a categorization quantity." Here we reach a completely different conclusion from [1], which we now elaborate.

First, we did not claim that the discrimination of healthy and pathologic groups can be obtained only by this new measure. Many measurements can be useful indicators for this purpose. In our Letter, we cited a major review article (Ref. [12] of [2]) where the utility of conventional statistics of heart rate variability is discussed. Our statement was that the categorization approach based on the dissimilarity index can provide "new quantitative information that is not measured by conventional heart rate variability techniques." We presented this new information in the Letter and also discussed quantitative ways to support this claim (see Ref. [12] of [2]). Therefore, the suggestion that the essential result of our Letter is simply the discrimination of physiologic and diseased groups is misleading. We provide two further examples to illustrate this point.

The first example is to compare Fig. 3 of [2] with Fig. 1 of [1], which shows different groups in distinct regions of the mean and standard deviation (SD) plot. Similar distinctions have been reported in previous studies (see Ref. [12] of [2] and references therein). In contrast, Fig. 3 of [2] provides new information about the relationship among these groups, namely, that the relative deviation of pathologic and aging groups from healthy young can be organized on a phylogenetic tree. This type of information cannot be revealed by the approach of Kraskov *et al.*

The second example is the following: A closer examination at Fig. 1 of [1] reveals that although the mean heart rate of the healthy young group is significantly different from the congestive heart failure (CHF) group, many data points from subjects in these two groups overlap. Consider selecting a subset that includes the five subjects with highest mean interbeat intervals in the CHF group and the five with lowest mean interbeat intervals in the healthy young group. These ten subjects are not distinguishable by their mean and SD. However, the phylogenetic tree based on our similarity index can clearly separate them (Fig. 1). This simple example demonstrates that our similarity index does indeed extract information not contained in conventional moment statistics.

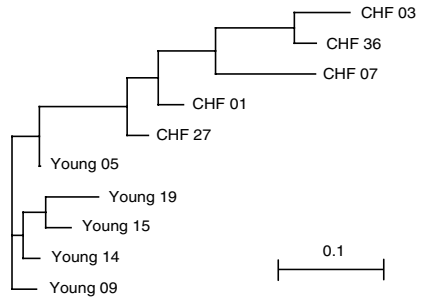

FIG. 1. Two subgroups were selected from the five subjects with the highest mean interbeat intervals (843.50 ms) in the congestive heart failure (CHF) group and the five with the lowest mean interbeat intervals (818.34 ms) in healthy young group. The phylogenetic tree based on our similarity index can correctly separate them into two different groups, despite overlap of the means and standard deviations of their heart rates.

In addition to these two main comments, Kraskov *et al.* also suggested that most atrial fibrillation (AF) time series can be distinguished from artificial random noise by their nonzero autocorrelation function. As previously reported (see Ref. [7] in our Letter), AF time series have statistical properties similar to white noise on shorter time scales (< 200 s). For longer time scales, the data are often nonstationary (the mean heart rate drifts away from a constant value). Therefore, the nonzero autocorrelation function is likely to be caused by artifact of applying autocorrelation analysis to nonstationary data.

Finally, we emphasize that our method provides a generic approach to classifying information-carrying symbolic sequences not limited to heart rate time series [3]. Importantly, most other statistical techniques cannot be implemented directly on different kinds of symbolic sequences without major modifications.

Albert C.-C. Yang,[1] Shu-Shya Hseu,[2] Huey-Wen Yien,[2] Ary L. Goldberger,[1] and C.-K. Peng[1]
[1]Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, Massachusetts 02215, USA
[2]Taipei Veterans General Hospital, Taipei, Taiwan

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