Hierarchical Structure in Healthy and Diseased Heart Rate Variability in Humans

Emily S.C. Ching\(^1\), D.C. Lin\(^2\) and C. Zhang\(^1\)

\(^1\)Department of Physics, The Chinese University of Hong Kong, Shatin, Hong Kong.
\(^2\)Department of Mechanical and Industrial Engineering, Ryerson University, Toronto, Canada.

It is shown that the heart rate variability (HRV) in healthy and diseased humans possesses a hierarchical structure of the She-Leveque (SL) form. This structure, first found in measurements in turbulent fluid flows, implies further details in the HRV multifractal scaling. The potential of diagnosis is also discussed based on the characteristics derived from the SL hierarchy.

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The heart beat interval in humans is known to exhibit fluctuation which is referred to as heart rate variability (HRV). Power spectrum analysis of the fluctuation revealed a 1/f-like scaling \([1]\). Recent studies indicated that healthy human HRV exhibits even higher complexity which can be characterized by multifractal scaling \([2, 3]\). In contrast, HRV in the pathological state such as congestive heart failure exhibits more monofractal-like scaling \([2]\). The change of the HRV 1/f law in congestive heart failure is consistent with this result \([3]\). Such a monofractal-monofractal transition was also reported in parasympathetic nervous system (PNS) blockade experiment \([3]\). Hence, further studies revealed that the monofractal HRV have properties analogous to those found in fluid turbulence \([3]\). However, there is little understanding beyond the phenomenological description of multifractal HRV.

In this paper, we exploit further the analogy of HRV to fluid turbulence and show the existence of a hierarchical structure in healthy and diseased HRV. This structure allows us to model the multifractality of HRV and make conjecture to the heart beat dynamics responsible for the multifractal scaling. The hierarchy, first proposed by She and Leveque (SL) to understand the statistical properties of turbulent flows, provides a successful framework to discuss and characterize the deviation from Kolmogorov monofractal scaling in fluid turbulence \([6]\). When applied to study HRV, the SL hierarchy provides a model structure which possesses two advantages: (a) it simplifies the functional description of the multiscaling by using a maximum of only three parameters, and (b) it contains predictive power for HRV scaling in physiological states related to PNS withdrawal. One immediate implication is the potential use of this notion in applications such as diagnosis.

Let the beat-to-beat RR interval (RRi) be \(r(t)\), where \(t\) is the beat number, and its increment be \(\Delta r(\tau) = r(t + \tau) - r(t)\). The SL hierarchy implies, for a range of \(\tau\),

\[
\left[ \frac{S_{p+2}(\tau)}{S_{p+1}(\tau)} \right] = A_p \left[ \frac{S_{p+1}(\tau)}{S_p(\tau)} \right]^\beta \left[ \frac{S^\infty(\tau)}{1} \right]^{1-\beta}.
\]

(1)

Here \(0 < \beta < 1\) is a parameter of the hierarchy, \(A_p\), a function of \(p\), \(S_p(\tau) = \langle |\Delta r(\tau)|^p \rangle\), the \(p\)-th order moment of \(|\Delta r(\tau)|\) denoted as the \(p\)-th order RRi structure function, \(S^\infty(\tau) = \lim_{\tau \to \infty} \frac{S_{p+1}(\tau)}{S_p(\tau)}\) and \(\langle \cdot \rangle\) denotes statistical average. Since \(S^\infty(\tau)\) is dominated by the statistics of large \(\Delta r(\tau)\), it characterizes the most intense fluctuation in HRV. Moreover, given the empirical law \(S_p(\tau) \sim \tau^{\zeta(p)}\) in HRV \([3]\), the hierarchy \([1]\) implies \([2]\) the scaling model

\[
\zeta(p) = h_0 + C(1 - \beta^p)
\]

(2)

where \(h_0\) and \(C\) are two other parameters of the hierarchy. It follows from \([1]\) and \([2]\) that \(S^\infty(\tau) \sim \tau^{h_0}\). A nonlinear functional dependence of \(\zeta(p)\) on \(p\) indicates multifractal scaling. Thus, the parameter \(\beta\) measures the degree of multifractality. In particular, \(\beta \to 1\) leads to monofractal scaling. In the multifractal description of fluid turbulence, the parameter \(C\) can be shown to be the codimension of the most intense structure of the flow \([4]\). Since it is not yet possible to write down the equation of motion for long-term cardiovascular dynamical system, we assume a working definition for \(C\) as the "codimension parameter" of the signal.

We follow the procedure developed in Ref. \([4]\) to check whether the RRi data possess a SL hierarchical form. This approach, based on the scaling property implied by the hierarchy, the so-called generalized extended self-similarity (GESS) in fluid turbulence \([3, 4]\), describes a power-law relationship between the normalized structure functions:

\[
\frac{S_p(\tau)}{[S_q(\tau)]^{p/n}} \sim \left\{ \frac{S_q(\tau)}{[S_q(\tau)]^{q/n}} \right\}^{\rho_n(p,q)}
\]

(3)

In the case of SL hierarchy, the exponents \(\rho_n(p,q)\) depends only on the model parameter \(\beta\):

\[
\rho_n(p,q) = \frac{n(1 - \beta^q) - p(1 - \beta^n)}{n(1 - \beta^n) - q(1 - \beta^p)}
\]

(4)
It follows that
\[
\Delta \rho_n(p + \delta p, q) = \beta^{\delta p} \Delta \rho_n(p, q) - \frac{\delta p(1 - \beta^n)(1 - \beta^{\delta p})}{n(1 - \beta^n) - q(1 - \beta^n)}
\]
(5)
where \(\Delta \rho_n(p, q) \equiv \rho_n(p + \delta p, q) - \rho_n(p, q)\). One can then plot \(\Delta \rho_n(p + \delta p, q)\) vs \(\Delta \rho_n(p, q)\) to check (5) and hence the validity of the SL hierarchy. We use several databases to perform the calculations (3) and (5). The first database (DB1) contains 10 sets of daytime ambulatory RRi recordings taken from healthy young adults. The second database (DB2) contains 18 sets of daytime normal sinus rhythm RRi data downloaded from public domain. We also analyze RRi data from congestive heart failure patients (DBCHF) from the same public domain to study the intricacy of the hierarchy.

Except for a few cases where excessive ectopic beats in the RRi data complicates the calculation of \(S_p(\tau)\), and were therefore discarded from the analysis, GESS is found in both healthy and CHF HRV. The exponent \(\rho_n(p, q)\) is then estimated from (5) and used in (2) to calculate \(\Delta \rho_n(p, q)\). Typical \(\Delta \rho_n(p + \delta p, q)\) vs \(\Delta \rho_n(p, q)\) plots are shown in Fig. 1. The observed linear trend implies (5). Hence, SL hierarchy is compatible with the multifractal scaling in HRV. From such plots, we estimate the value of \(\beta\) simultaneously from the slope and the intercept of the fitted straight lines. The results are given in Fig. 2a. The \(\beta\)'s from healthy HRV (DB1, DB2) cluster in the range \([0.65, 0.85]\) with those \(\zeta(p)\) showing less curvature being characterized by larger \(\beta\) values (Fig. 1). The \(\beta\)'s from DBCHF are generally larger in values due to the mono-fractal-like scaling.

To gain insight of the hierarchy, She and Wamire (SW) arrived at the hierarchy using multiplicative random cascade. Their cascade consists of two dynamic components. One is the basic component that generates the singular dynamics over a continuum of scales. It can be shown that this dynamical component gives rise to the scaling term \(h_{\delta p}\) in (2). SW's cascade contains an extra component, which they called the “defect dynamics” (DD), that modulates the singular structure through the multiplication of \(\beta\) in discrete steps. It can be shown that this dynamical component contributes to the nonlinear term \(C(1 - \beta^p)\) in (2). To apply SW's interpretation requires some clarification since continuous scale invariance does not exist in HRV, due to the fact that RRi fluctuation between heart beats cannot be defined. This suggests a dominant DD in the generation of the multifractal scaling of HRV and a scaling model with \(h_0 \sim 0\). Equivalently, this implies a hierarchy with a \(\tau\)-independent \(S^\infty\). Since \(S^\infty\) cannot be directly calculated, to verify such a model we first re-write (1) as
\[
S_p(\tau) \sim S^\infty(\tau)^\mu(p, q)
\]
(6)
where \(\mu(p, q) \equiv (1 - \beta^p)/(1 - \beta^n)\). We then form the quotient of (6) at distinct values of \(\tau\) and \(\tau_0\), which, after some algebra, yields
\[
\log_2 \frac{S^\infty(\tau)}{S^\infty(\tau_0)} = \log_2[S_p(\tau)/S_p(\tau_0)] - \mu(p, q) \log_2[S_q(\tau)/S_q(\tau_0)]/p - \mu(p, q) \equiv F_{p,q}(\tau, \tau_0).
\]
(7)
Hence, \(F_{p,q}(\tau, \tau_0)\) is independent of \(p\) and \(\tau\) and a \(\tau\)-independent \(S^\infty(\tau)\) implies a “constant” \(F_{p,q}(\tau, \tau_0)\) over a range of \(\tau\) and \(\tau_0\) values. Figure 3 shows \(F_{p,q}(\tau, \tau_0)\) for healthy and CHF HRV. It is seen that the condition \(h_0 \sim 0\) can be statistically ascertained and that \(\zeta(p) \sim S(1 - \beta^p)\). Given this, \(C\) is obtained by averaging \(\zeta(p)/(1 - \beta^n)\) over a range of \(p\) and its result has been shown in Fig. 2b. Moreover, \(C\), as a function \(\beta\), shows an increasing trend as \(\beta \rightarrow 1\) (Fig. 4). This functional relationship is consistent with the observations \(h_0 \sim 0\) and that \(\zeta(p)\) becomes almost proportional to \(p\) as \(\beta \rightarrow 1\). It can also be inferred from the earlier experimental studies, as we now explain.

Recall that the fractal dimension \(D(h)\) of the set with a local scaling exponent \(h\) is related to \(\zeta(p)\) through a Legendre transform:
\[
D(h) = \min_p [ph + d - \zeta(p)]
\]
(8)
where \(d\) is the dimension of the embedding space. From (2) and with \(h_0 \approx 0\), \(D(h)\) can be explicitly obtained as:
\[
D(h) = d - C + \left[\frac{1 + \ln C + \ln(\ln 1/\beta)}{\ln(1/\beta)}\right] h - \frac{h \ln h}{\ln(1/\beta)}.
\]
(9)
Let \(h^*\) be the scaling exponent of the singular set with largest dimension, i.e., \(D(h^*)\) is the maximum. For HRV, \(h^*\) was found to increase its value from the multifractal-like scaling in healthy state to the mono-fractal-like scaling in the diseased and pathological states. Using (9), \(h^*\) is derived explicitly as
\[
h^* = C \ln(1/\beta).
\]
(10)
If $C$ is constant, $h^*$ decreases as monofractal scaling is approached ($\beta \to 1$), which contradicts what was observed. In order for $h^*$ to increase as $\beta \to 1$, $C(\beta)$ must diverge as $1/\ln(1/\beta)$. Indeed, we find that the dependence of $C$ on $\beta$ can be well described by $0.2\beta/\ln(1/\beta)$ (Fig. 4). Thus we have the result $h^* \sim 0.2\beta$ with $h^*$ increasing with $\beta$ in accord with the experimental observations. Finally, the asymptotic behaviour of $C$ (as $\beta \to 1$) presents a more favorable condition for diagnosis: i.e., the more monofractal-like scaling falls into the range with larger “separation” of the $C$ values (see also Fig. 2b).

In summary, we show that a hierarchical structure of the SL form exists in the healthy and diseased HRV. This property allows us to model the multifractal HRV in terms of only two parameters $C$ and $\beta$. Interestingly, $C$ and $\beta$ are related by an empirical law captured in Fig. 4. This finding is important for two reasons. First, the empirical law appears universal and is capable of describing both healthy and CHF data. Second, the divergence of $C$ as $\beta \to 1$ implies potential in diagnosis using the hierarchical structure. To find a model that is compatible with the current finding, we adopted SW’s cascade which leads to further implications beyond the phenomenological description of multifractal HRV scaling. This model is appealing in that it contains a modulating component (DD) acting on the singular dynamics to “tame” the fluctuation (since $\beta < 1$.) Its effect reminds us of the function of feedback regulation in biological systems. Hence, the SW’s model provides a concrete example of how (additive) feedback mechanism may be integrated multiplicatively in a cascading structure to produce the observed HRV phenomenology. Further experiments will be needed to test and quantify these possibilities in more detailed physiological terms.

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FIG. 1: Typical $\Delta \rho_n(p + \delta p, q)$ vs. $\Delta \rho_n(p, q)$ plots for (a) healthy HRV and (b) CHF HRV with $\delta p = 0.2$. We used $q = 1$ and $n = 2$ for healthy HRV and $q = 0.8$ and $n = 1.2$ for CHF HRV. The arrow direction indicates the increasing $p$ direction. The estimated slopes for the shown cases are $\beta^{(p)} = 0.9422$ and $0.9881$, respectively. Hence, $\beta \sim (0.9422)^5 = 0.7425$ and $(0.9881)^5 \sim 0.9491$, respectively. The insets show the corresponding $\zeta(p)$. It is seen that a large $\beta$ in CHF HRV implies a $\zeta(p)$ with less curvature, i.e., monofractal-like scaling.

FIG. 2: Estimated values for model parameters (a) $\beta$ and (b) $C$. Estimates from DB1, DB2 for 24 healthy subjects are given in circles and those from DBCHF for 30 congestive heart failure subjects are given in squares. Means and standard deviations in both cases are also shown by the bar-chart.
FIG. 3: Evidence of $\tau$-independent $S^\infty(\tau)$. $F_{p,2}(\tau,64)$ vs. $\log_2(\tau)$ from (a) a healthy subject ($p = 0.2 \sim 5$) and (b) a CHF patient ($p = 0.4 \sim 2.6$). The $\beta$ needed in the calculation of $\mu(p,q)$ (see 7) is obtained from that estimated by 4.

FIG. 4: $C$ vs. $\beta$ empirical law for healthy subjects (open circles) and congestive heart failure patients (solid circles). The solid line is the fit $C = 0.2\beta/\ln(1/\beta)$.