Complexity Measures: Entropy & Time Irreversibility

2006 Heart Rate Variability

HRV 2006

Techniques, Applications and Future Directions

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Objectives

- To discuss the relevance of measures of complexity to physiology
- To describe the uses and limitations of entropy-based measures of complexity, including Approximate Entropy (ApEn)/Sample Entropy (SampEn), and Multiscale Entropy (MSE)
- To introduce a multiscale measure of time irreversibility
- To describe the application of these metrics to clinical datasets in aging and heart disease and implications for modeling

Motivation for New Approaches

- A system's *complexity* will be reflected in the dynamical fluctuations generated by the *free-running* conditions

Complexity (healthy systems) > Complexity (pathologic systems)

- Healthy systems operating, far from equilibrium, have greater adaptability and functionality than pathologic systems, therefore

- Disease, aging, drug toxicities should degrade complexity

Challenges

What is ***complexity*** and how to measure it?

No consensus on definition!

Currently, a variety of entropy-based algorithms are used for computation, such as Approximate Entropy (ApEn) and Sample Entropy (SampEn)

Part 1: Entropy-based Complexity Measures

- Approximate Entropy* (ApEn):

  Natural logarithm of the relative prevalence of repetitive patterns of length *m* compared with those of length *m*+1

- Sample Entropy** (SampEn) - a refinement of ApEn

- ApEn and SampEn, both quantify the regularity of a time series. More irregular (less predictable), more "complex"

- Both widely used for physiologic and other data analysis

*Pincus SM. Proc Natl Acad Sci 1991;88:2297

** Richman JS, Moorman JR. Am J Physiol Heart Circ 2000;278:H2039

PhysioNet Tutorials

Multiscale Entropy Analysis (MSE)

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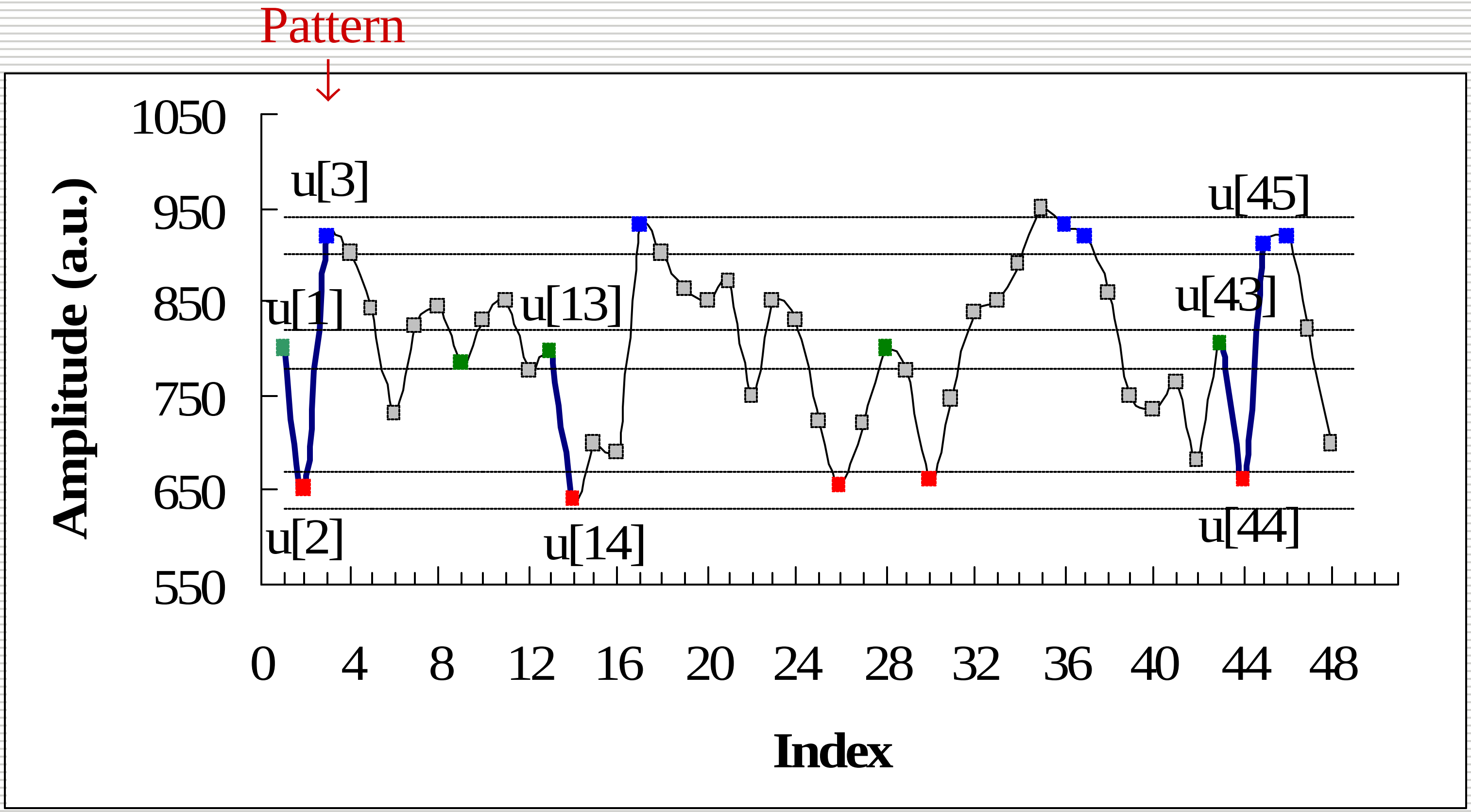
A detailed description of the multiscale entropy algorithm and its application can be found in:

- Costa M., Goldberger A.L., Peng C.-K. Multiscale entropy analysis of biologic signals. Phys Rev E 2005;**71**:021906.
- Costa M., Goldberger A.L., Peng C.-K. Multiscale entropy analysis of physiologic time series. Phys Rev Lett 2002; **89**:062102.

http://www.physionet.org/physiotools/mse/tutorial/

Sample Entropy (SampEn)

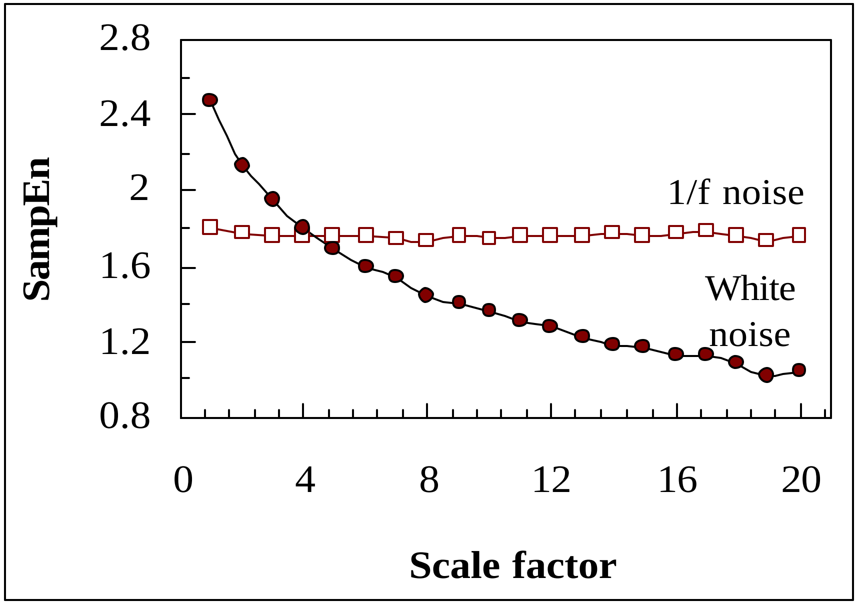
ln (patterns of length m) – ln (patterns of length m+1)



Other Problems

- ApEn (SampEn) indicate higher entropy for:
  1. Uncorrelated white noise than for correlated (1/*f*) noise
  2. Atrial fibrillation than for normal sinus rhythm
- However,
  1. 1/*f* noise is inherently more complex than white noise
  2. Atrial fibrillation may be physiologically less complex than normal sinus rhythm

Complexity: 1/f vs White Noise



- Entropy for coarse-grained white noise time series monotonically decreases with scale
- Entropy for coarse-grained 1/f time series remains constant for all scales consistent with the fact that 1/f noise has complex structures across multiple scales

1/f noise more complex than white noise

Strategy

- Meaningful complexity measure should account for multiple time scales inherent in healthy dynamics.

- Zhang* proposed such a measure. But, it does not readily apply to "real-world" time series since it requires a large amount of almost noise-free data.

- We** introduced a new **multiscale entropy** (MSE) method motivated by Zhang and Pincus.

* J Phys I 1991;1:971

** Phys Rev Lett 2002;89:068102 & Phys Rev E 2005; 71:021906

Multiscale Entropy (MSE) Algorithm

1. Coarse-grain the time series
2. Calculate SampEn for each coarse-grained series
3. Plot as a function of scale factor
4. Analyze the MSE curve profiles

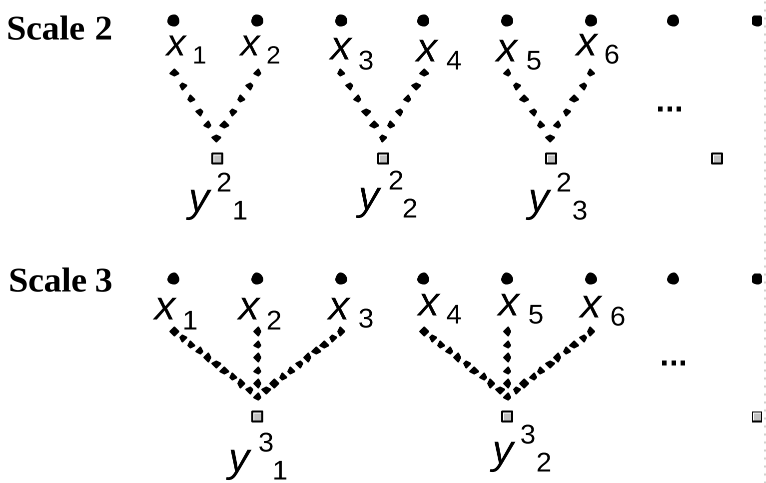
References:

M. Costa, A.L. Goldberger, C.-K. Peng. *Physical Review Letters* 2002;89:068102

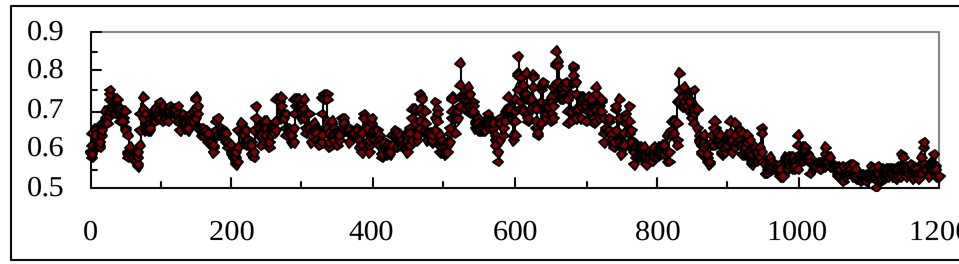
M. Costa, A.L. Goldberger, C.-K. Peng. *Physical Review E* 2005;95:198102

Coarse-graining Procedure

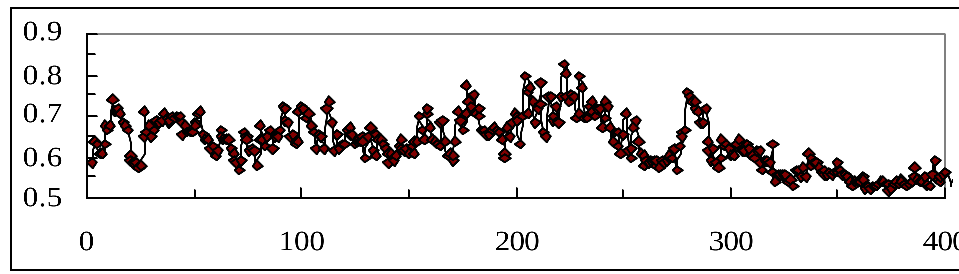
Coarse-graining schematic



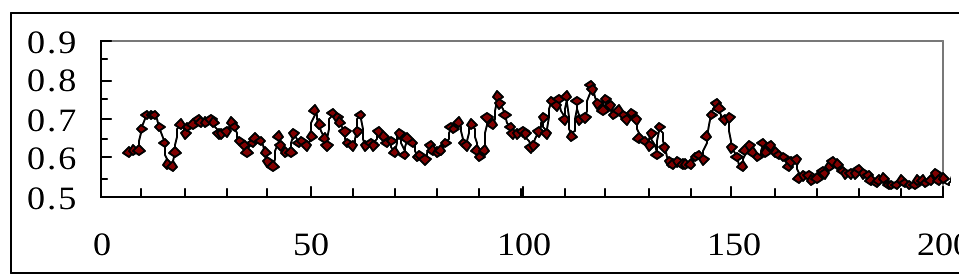
Scale 1: Original heartbeat time series



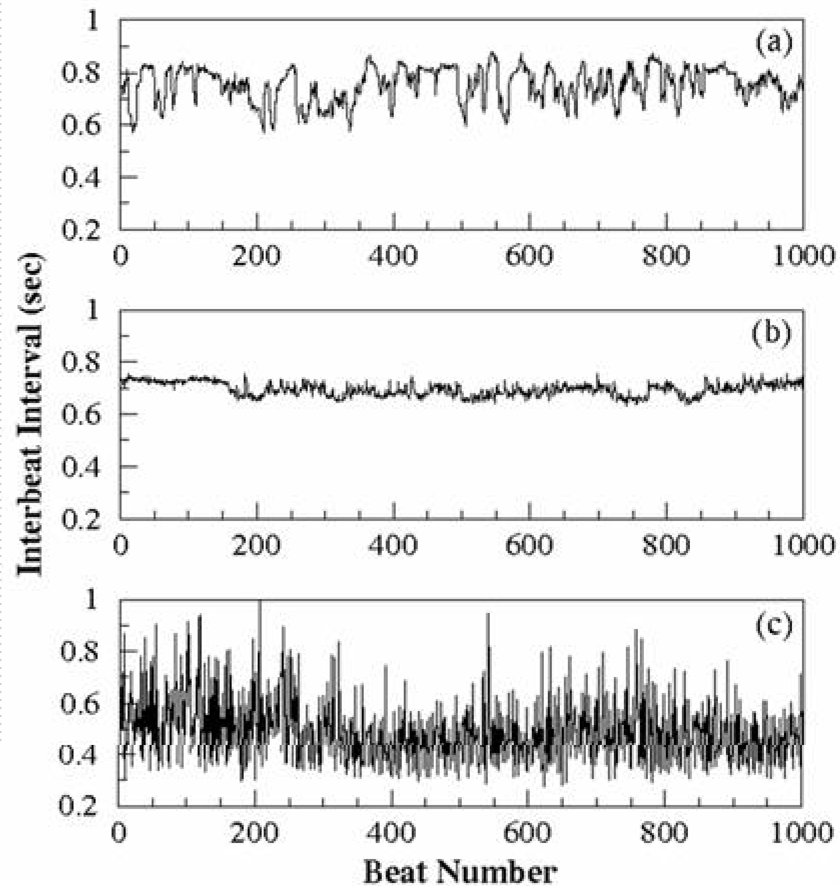
Scale 3

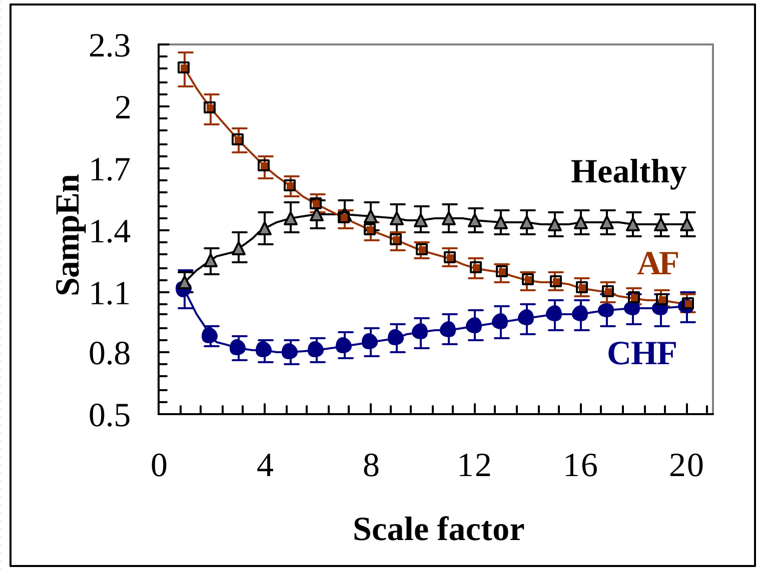


Scale 6



Multiscale Entropy (MSE) of Heart Rate Dynamics

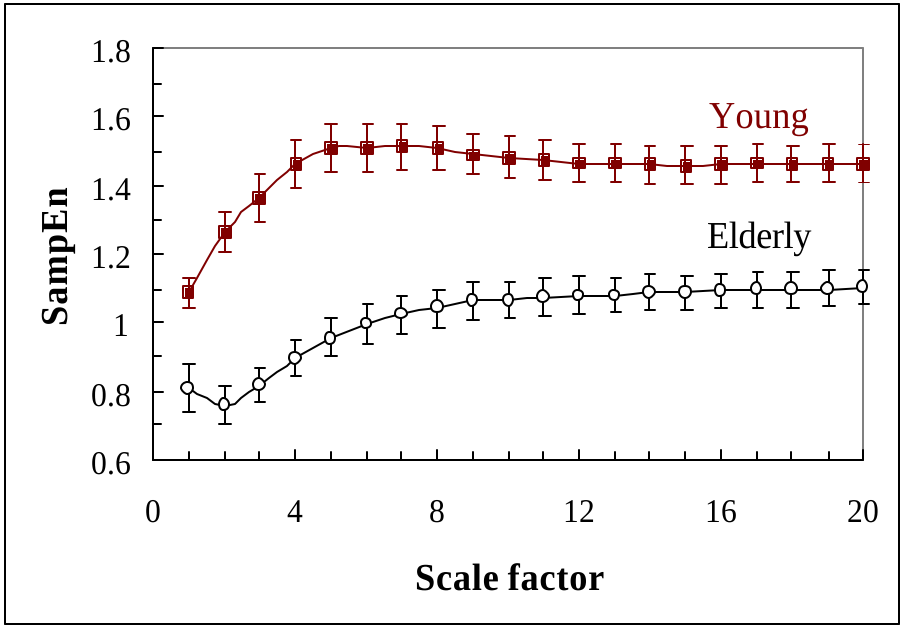




a) Healthy (n=18)
b) Congestive Heart Failure (CHF; n=15)
c) Atrial Fibrillation (AF; n=9)

MSE Analysis for Healthy Young vs. Elderly

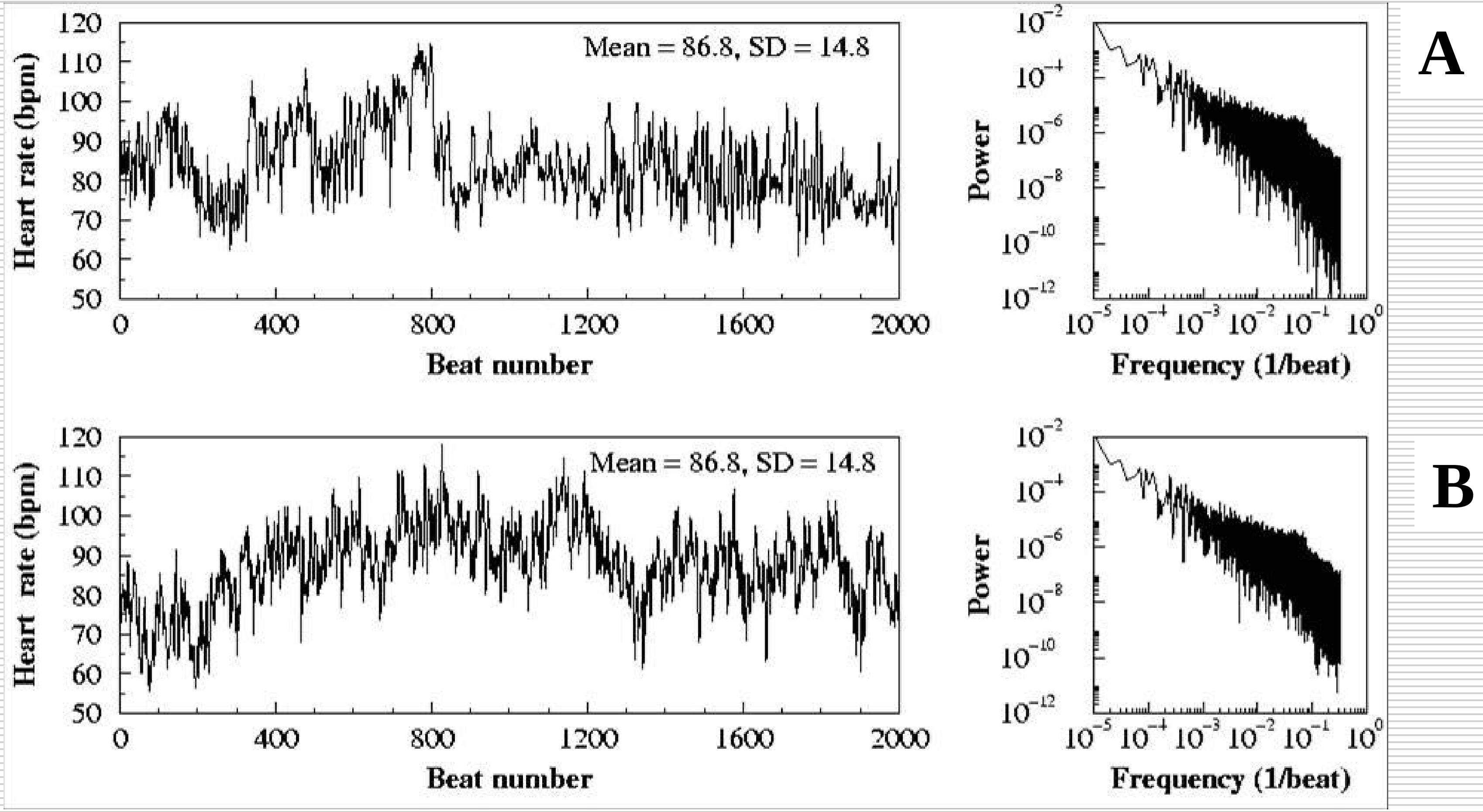
Complexity of heart rate variability decreases with aging



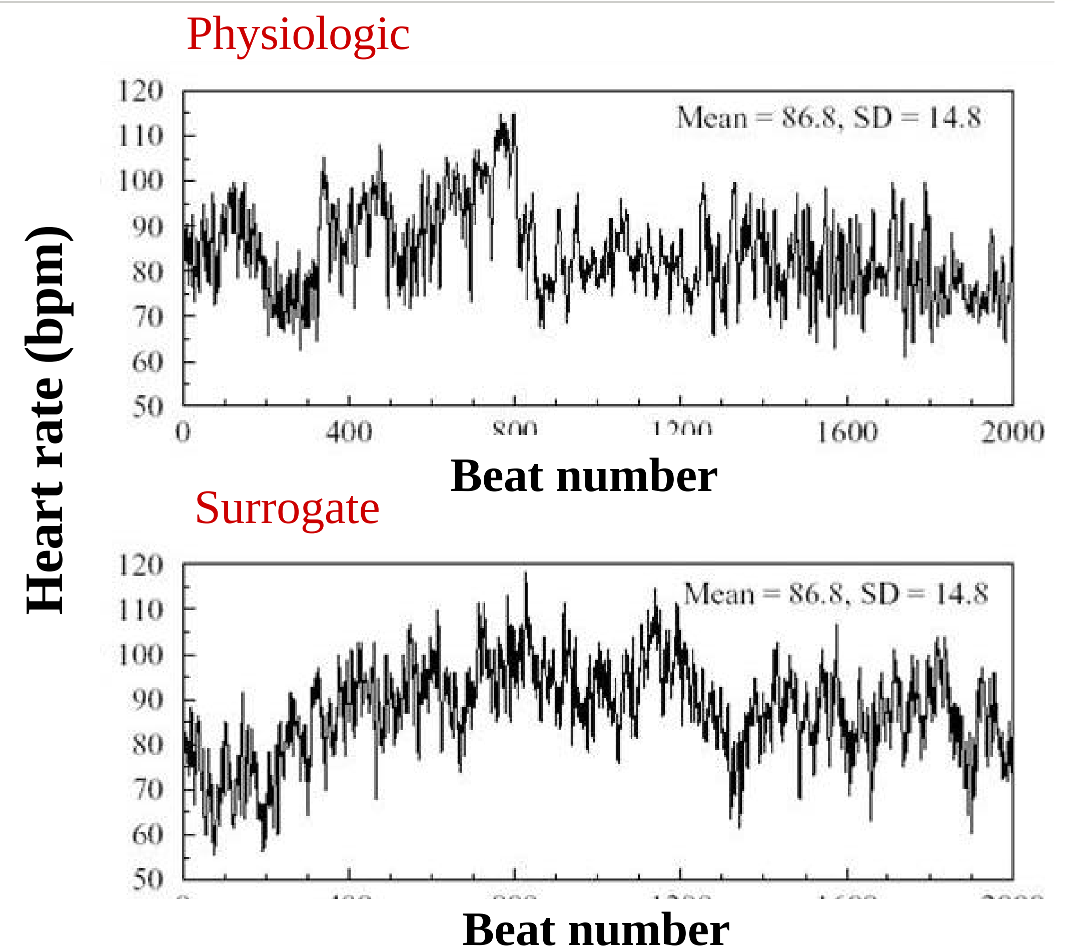
Elderly
N = 20; age 69±3

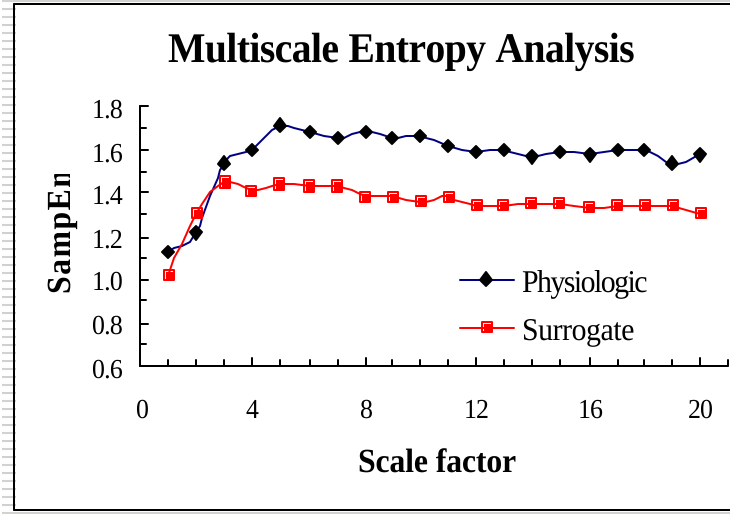
Young
N = 20; age 32 ±6

Beyond Traditional HRV: Which is Physiologic ?



MSE: Physiologic vs Surrogate Data





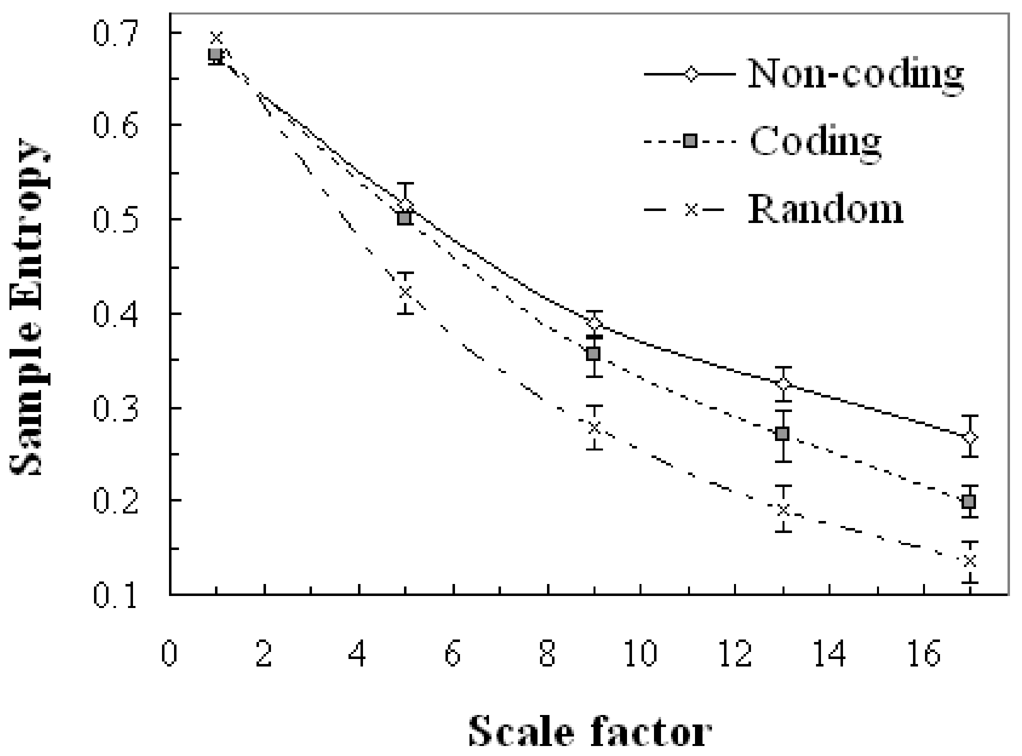
Thus, the physiologic time series is more complex than the phase randomized surrogate time series

Limitations

- Time series length
- Stationarity considerations
- Outlier effects
- Time irreversibility and certain other properties not accounted for

Other Applications: Binary Time Series

Are non-coding DNA sequences more complex than coding sequences?



Conclusions: Part 1

- Conventional complexity (single scale) measures => misleading results

  (e.g., atrial fibrillation more complex than sinus rhythm)

- Multiscale entropy (MSE)

  - 1/f noise more complex than white noise

  - healthy heart rate dynamics more complex than pathologic and aging

Pt. 2: Back to the Future:

Multiscale Time Irreversibility (Time Asymmetry)

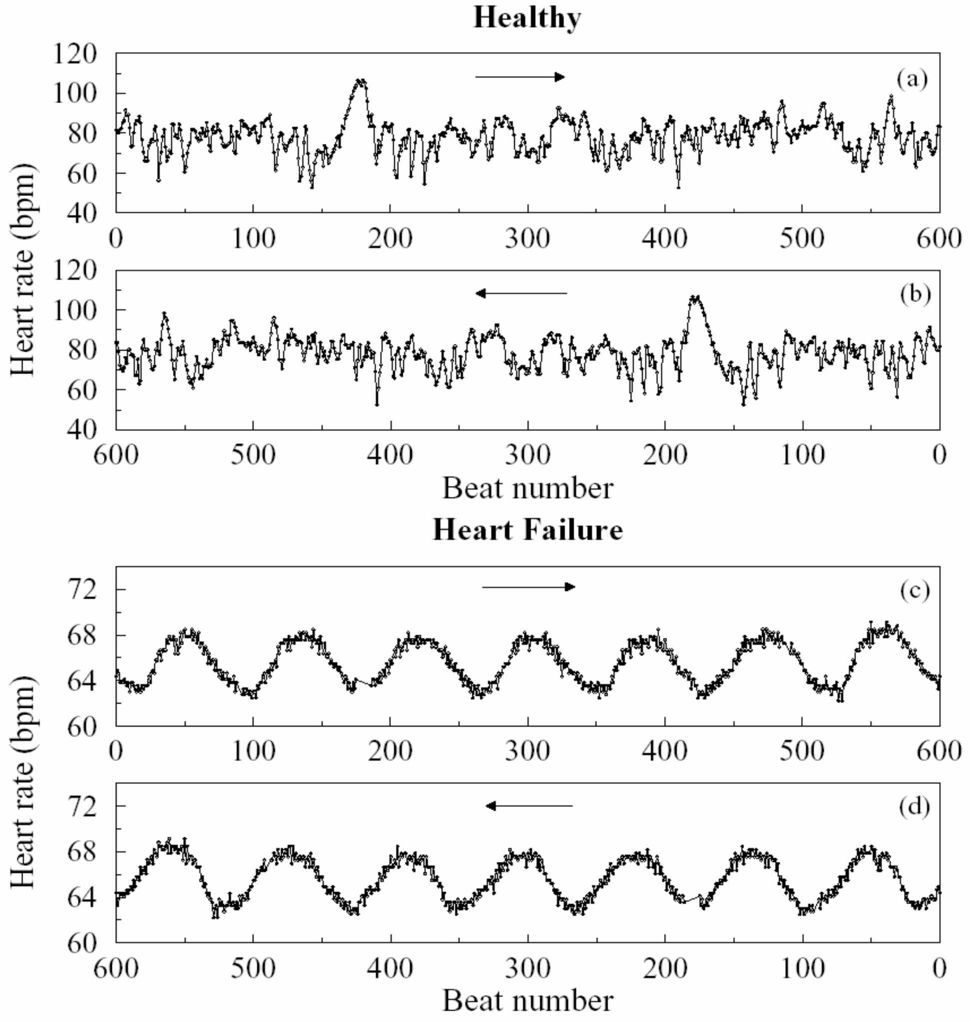
Multiscale Time Irreversibility (MTI): Background

- Definition: lack of invariance of the statistical properties of a signal under the operation of time reversal
- Fundamental property of non-equilibrium dynamics related to the unidirectionality of energy flow
- Current methods are single scale-based and lead to inconsistent results in physiologic signal analysis

Costa, Goldberger, Peng. Phys Rev Lett 2005;95:198102

Multiscale Time Irreversibility (MTI): Hypotheses

Healthiest vs Sickest



- Time irreversibility is greatest for healthy physiologic dynamics, which have the highest adaptability
- Time irreversibility decreases with aging and disease

Multiscale Time Irreversibility (MTI): Algorithm

- Coarse-grain time series
- Quantify the degree of temporal irreversibility for each coarse-grained time series
- Integrate the values of temporal irreversibility for each coarse-grained time series over a range of time scales

Time Irreversibility of Interbeat Interval Time Series

1. For each coarse-grained time series, we:
   i. Calculate the difference between consecutive data points
   ii. Calculate the percentage of positive $p(y_t > 0)$ and negative $p(y_t < 0)$ increments
   iii. The asymmetry index $A_i(\tau)$ is calculated by the equation:

$$A_i(\tau) = \frac{P(y_t > 0) \ln P(y_t > 0) - P(y_t < 0) \ln P(y_t > 0)}{P(y_t > 0) \ln P(y_t > 0) + P(y_\tau < 0) \ln P(y_t > 0)}$$

2. Over a range of time scales the asymmetry index is calculated by the equation: $\Sigma_{\tau=1} A_i(t)$.

Multiscale Time Asymmetry Measure

PHYSICAL REVIEW LETTERS

Broken Asymmetry of the Human Heartbeat: Loss of Time Irreversibility in Aging and Disease

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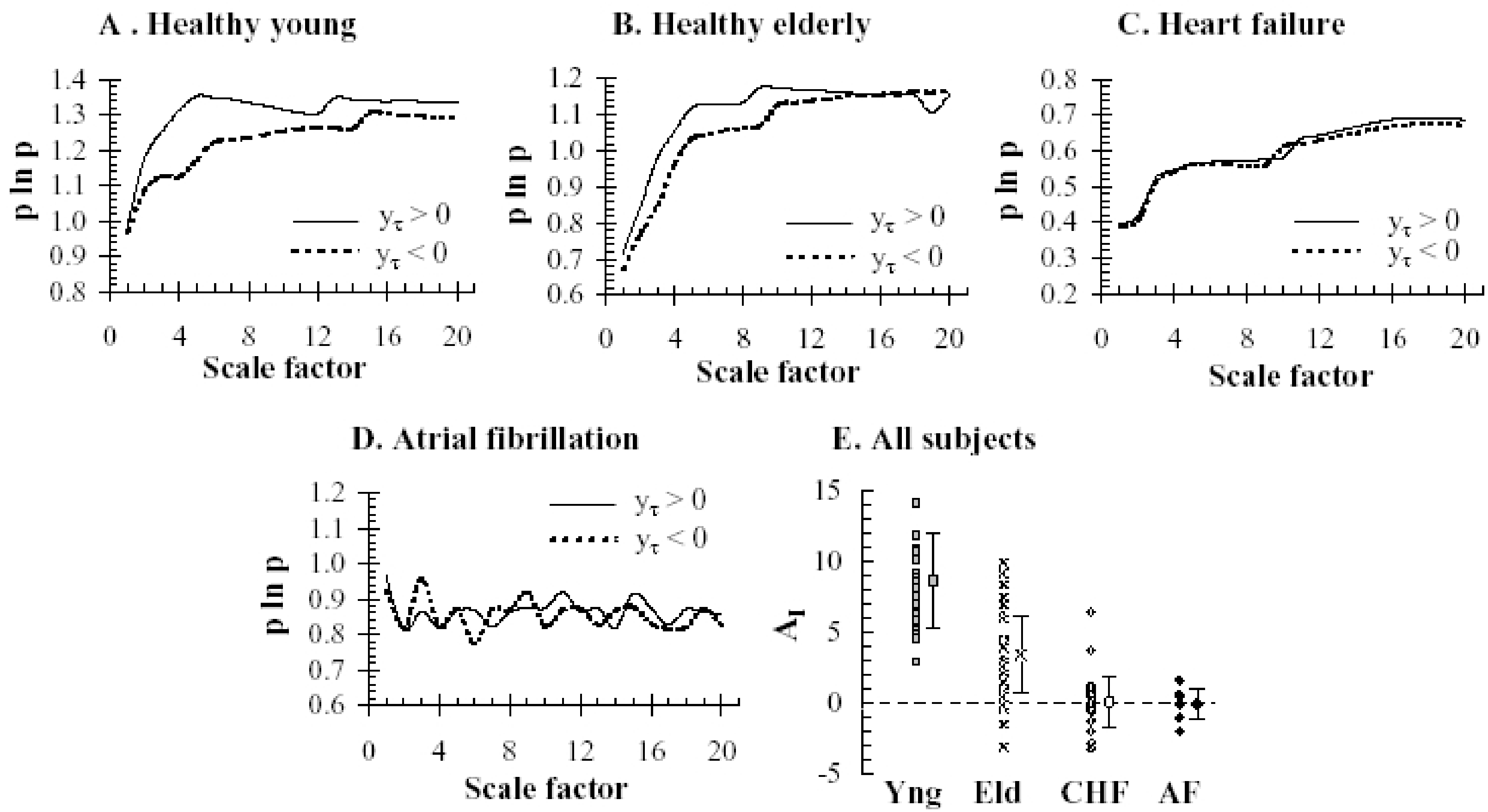
(Received 14 June 2005)

Time irreversibility, a fundamental property of nonequilibrium systems, should be of importance in assessing the status of physiological processes that operate over a wide range of scales. However, measurement of this property in living systems has been limited. We provide a computational method derived from basic physics assumptions to quantify time asymmetry over multiple scales and apply it to the human heartbeat time series in health and disease. We find that the multiscale time asymmetry index is highest for a time series from young subjects and decreases with aging or heart disease. Loss of time irreversibility may provide a new way of assessing the functionality of living systems that operate far from equilibrium.

Phys Rev Lett, 2005;95:198102.

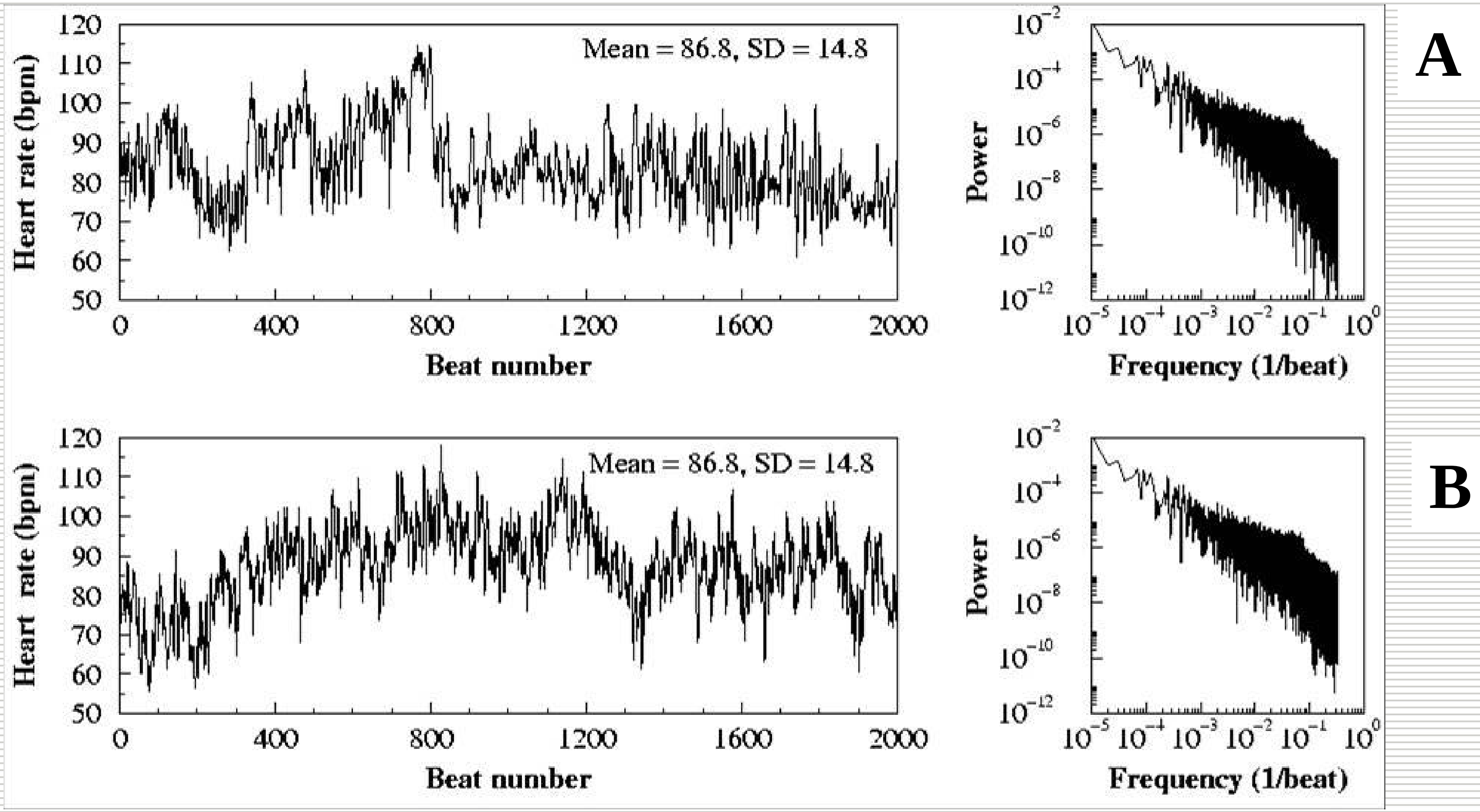
Time Irreversibility Analysis: Heart Rate Dynamics



Healthy (n = 26)
Congestive Heart Failure (n = 43)
Atrial Fibrillation (n = 9)

Data available at www.physionet.org

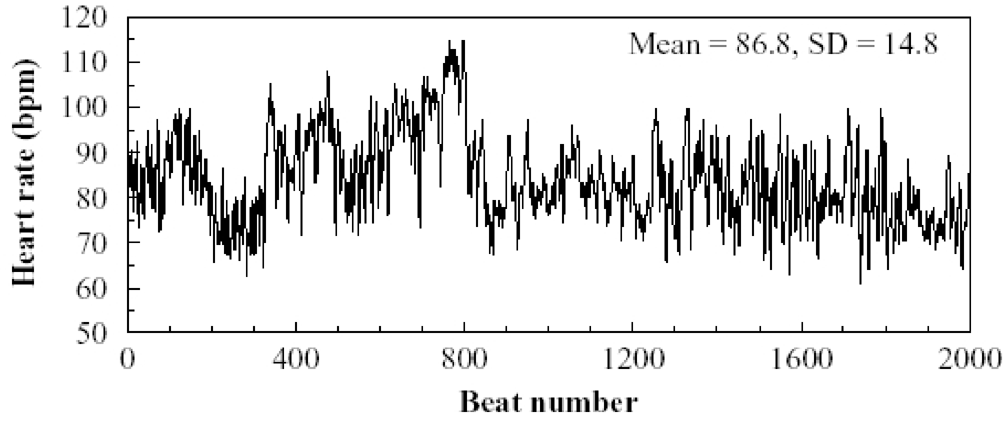
Beyond Traditional HRV: Which is Physiologic ?



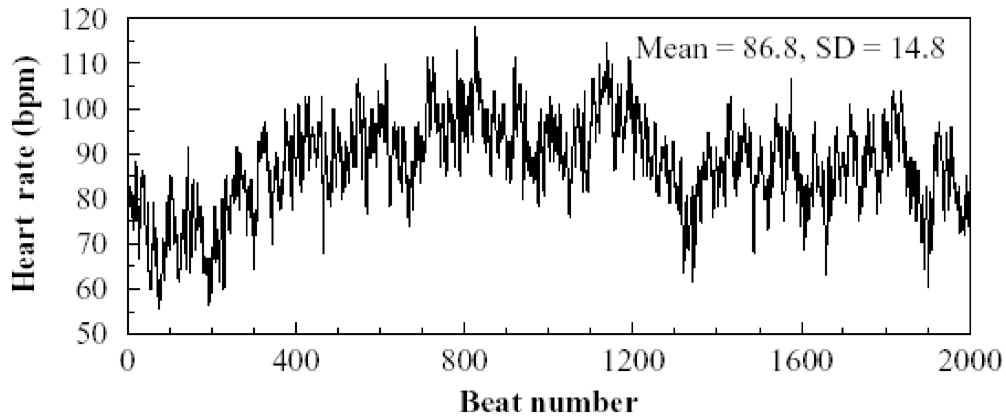
A: Physiologic B: Surrogate (phase randomized)

Applying New Multiscale Measures

A



B



Multiscale Time Asymmetry

- **Physiologic:**
  Asymmetry index = 3.4
- **Surrogate:**
  Asymmetry index = 0.5

A: Physiologic B: Surrogate (phase randomized)

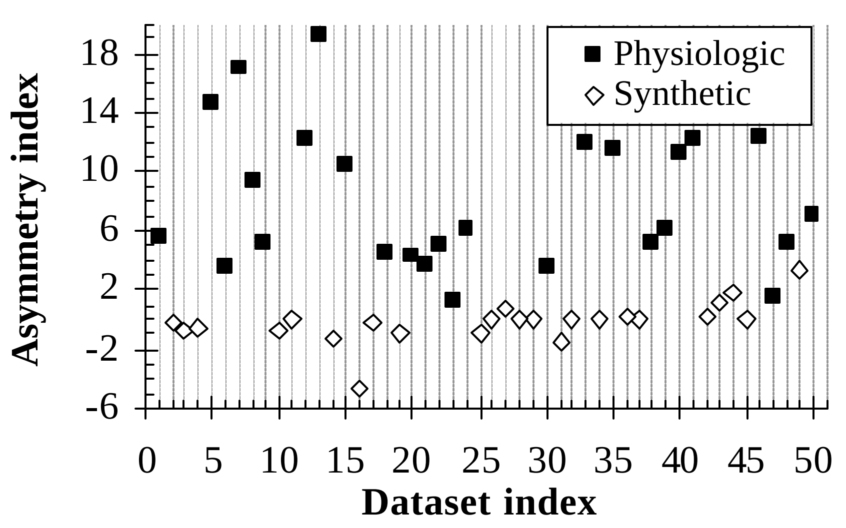
Thus, the physiologic time series is more complex and time asymmetric than the surrogate

Pt. 3: Modeling Implications

- Do current models of cardiac control account for time irreversibility and multiscale complexity properties of physiologic signals?

- We analyzed physiologic (n=26) and model generated (n=24) time series from Computers in Cardiology Conference (CinC)/PhysioNet Challenge 2002: Modeling RR Time Series (www.physionet.org)

Time Irreversibility: CinC/PhysioNet 2002 – Challenge



Physiologic heart rate signals are more time irreversible than model generated

Conclusions

- Multiscale entropy and time irreversibility probe fundamental features of complex variability
- Physiologic models need to account for these features and currently do not

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