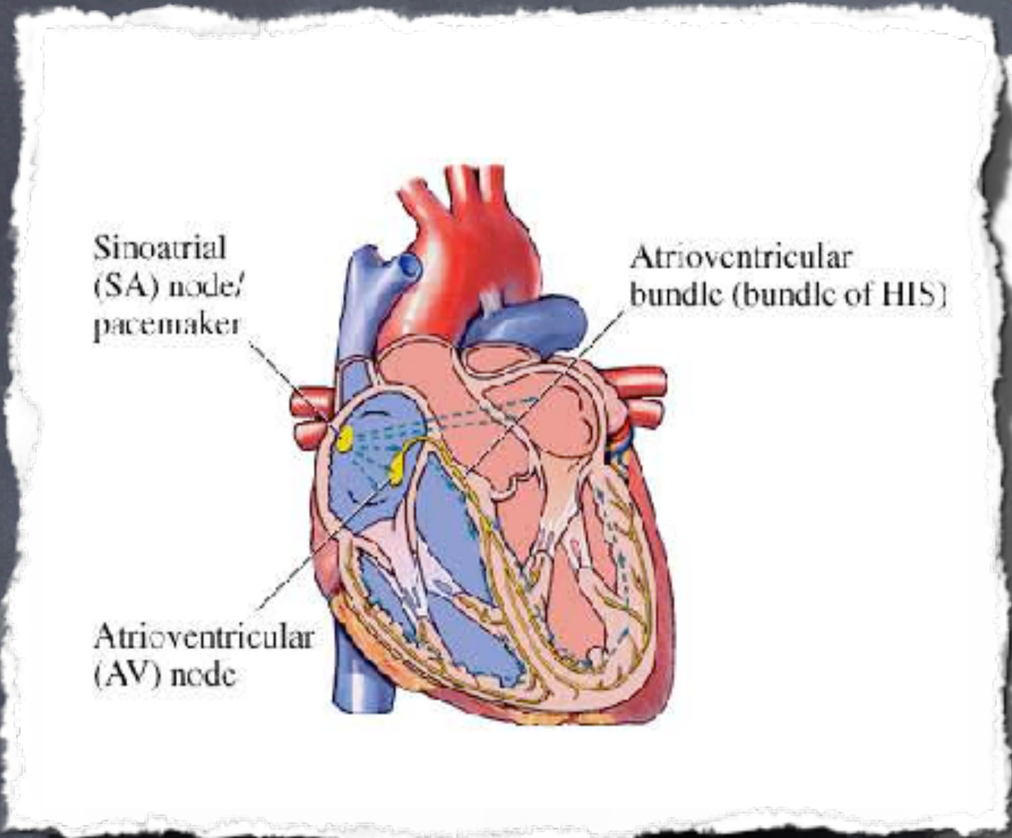
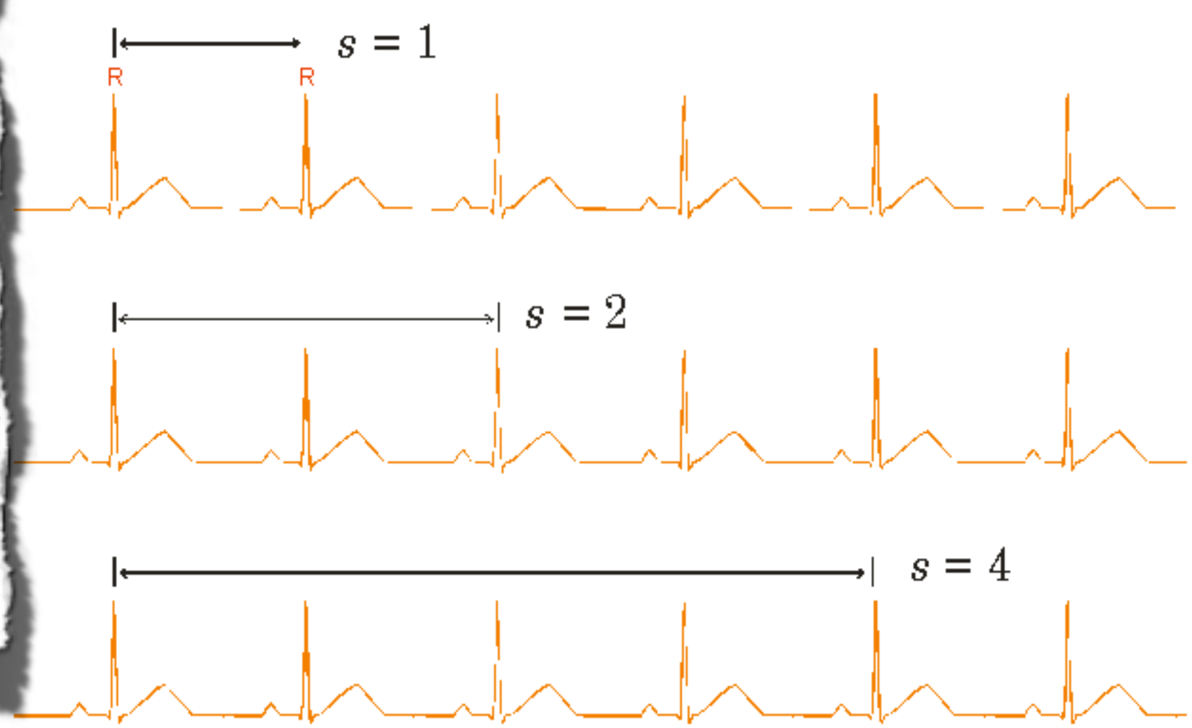
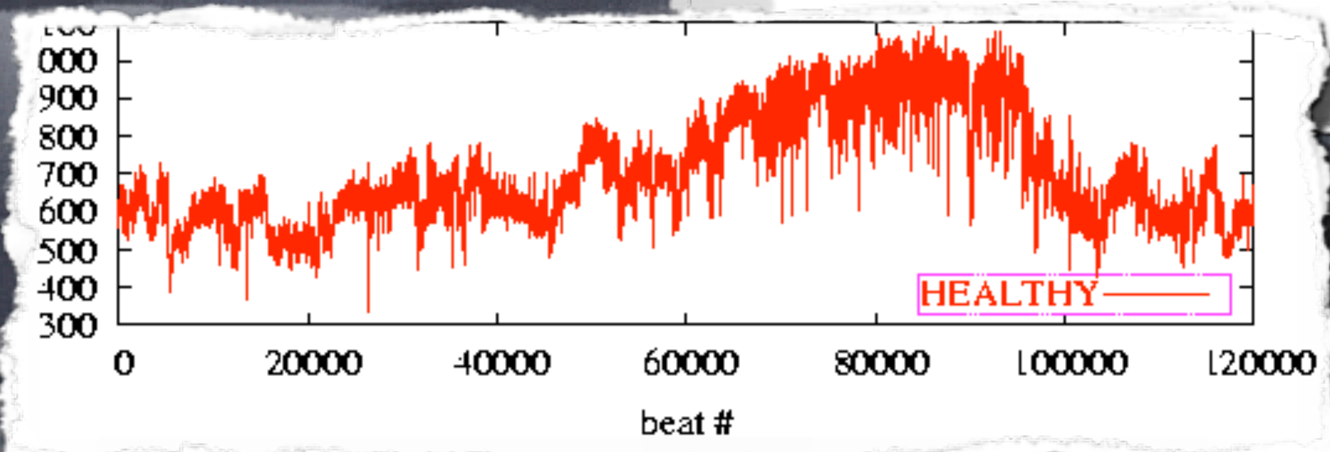
Is Complexity of Heart Rate Decreased or Increased in Congestive Heart Failure

Zbigniew R. Struzik
Graduate School of Education
Tokyo University

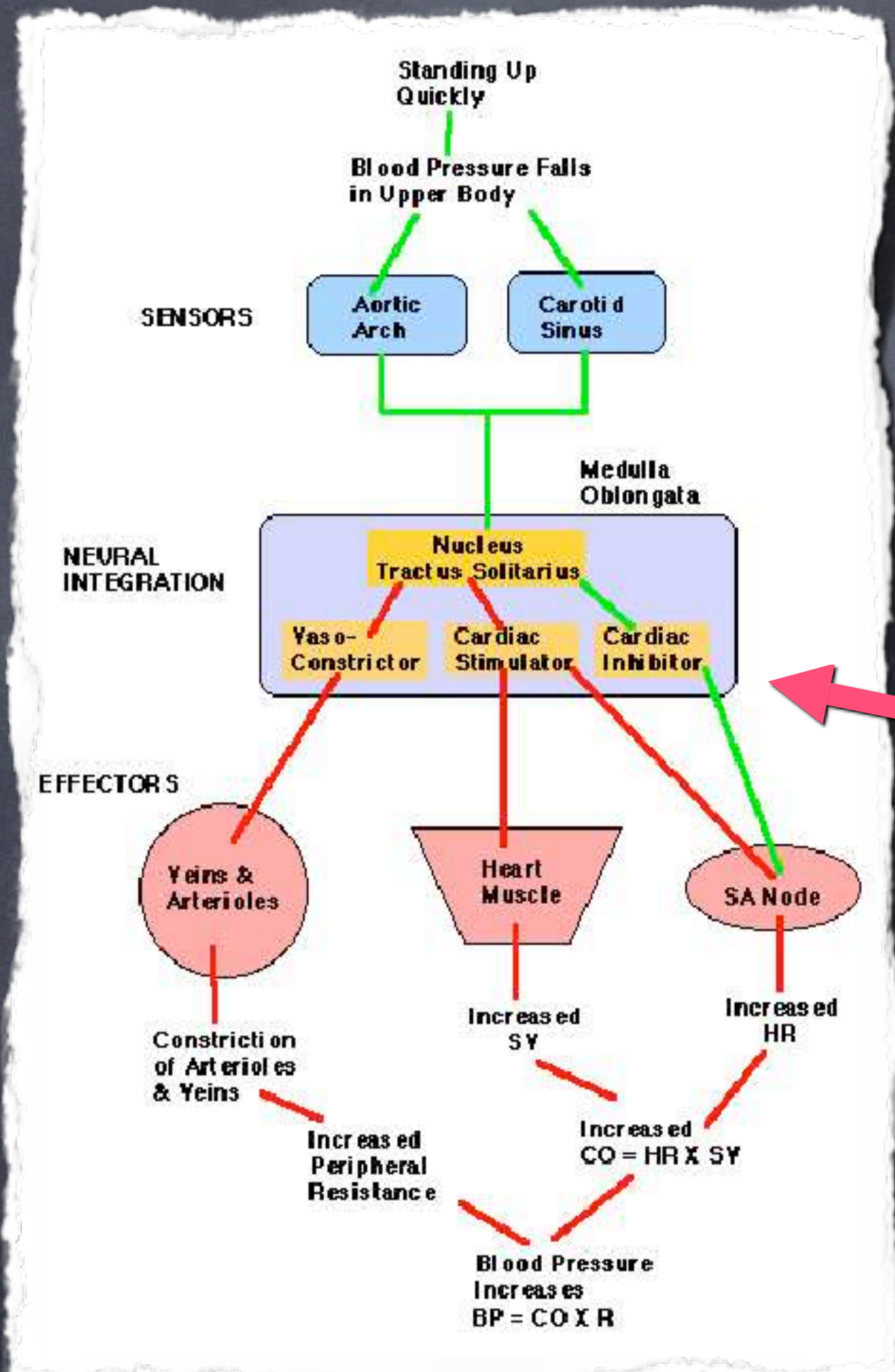
Heart rate interbeat intervals

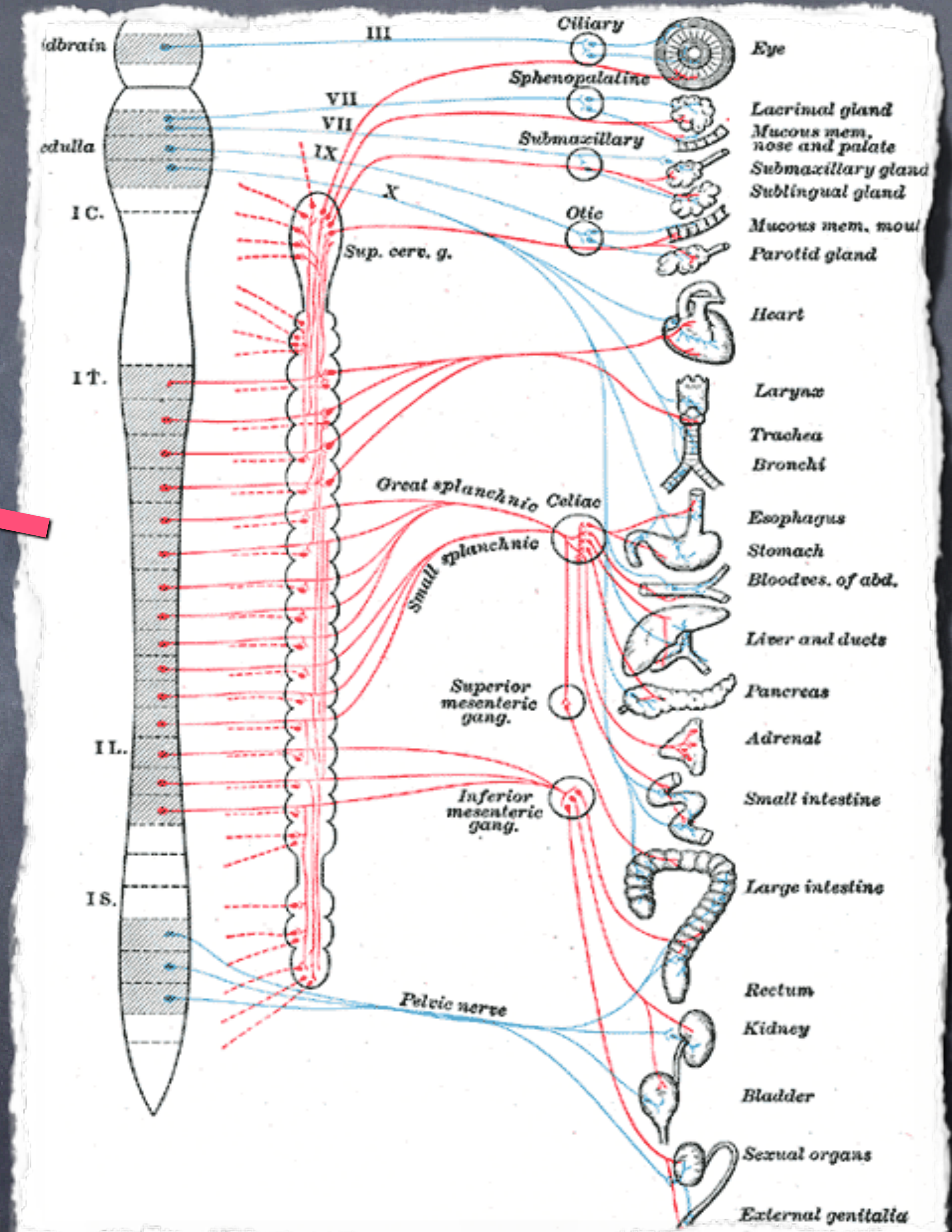






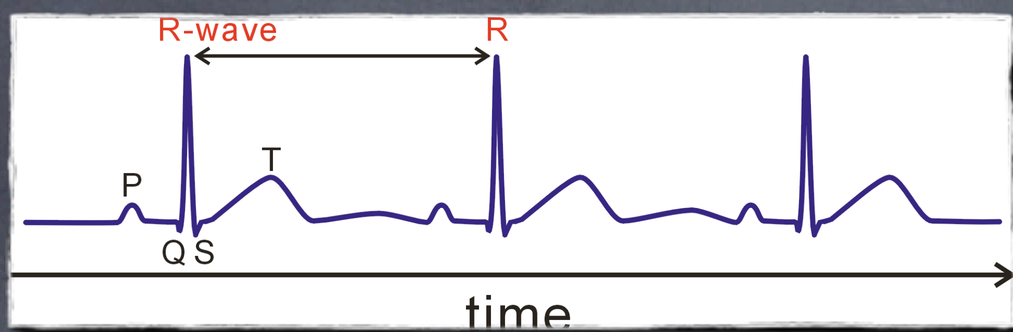
Autonomic regulation of heart rate



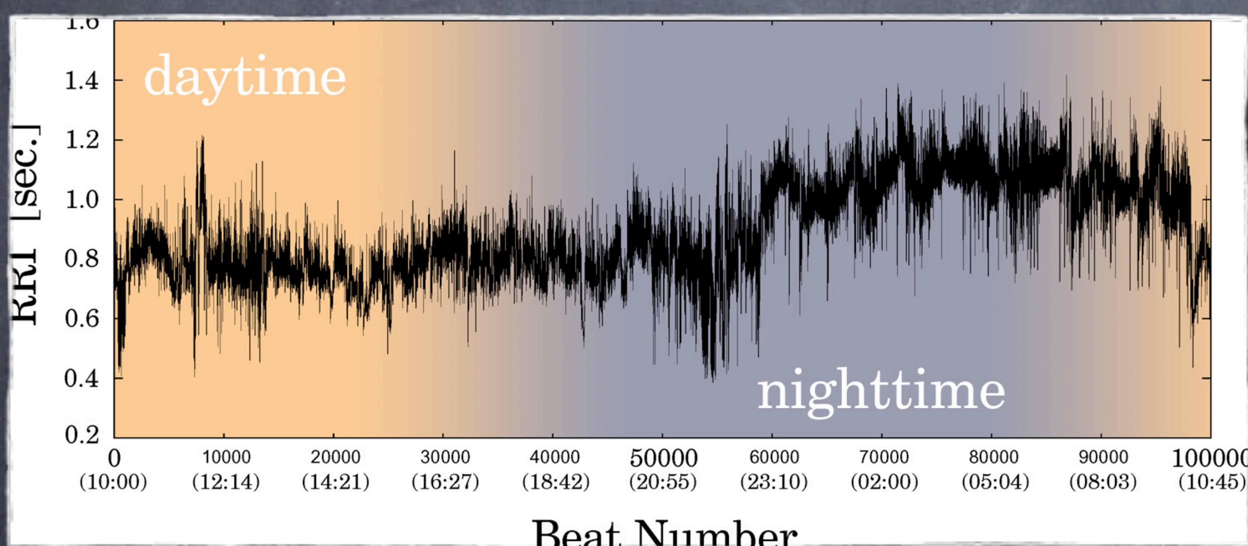


1/f scaling of heartbeat fluctuations, Kobayashi and Musha, IEEE-TBE, 1982

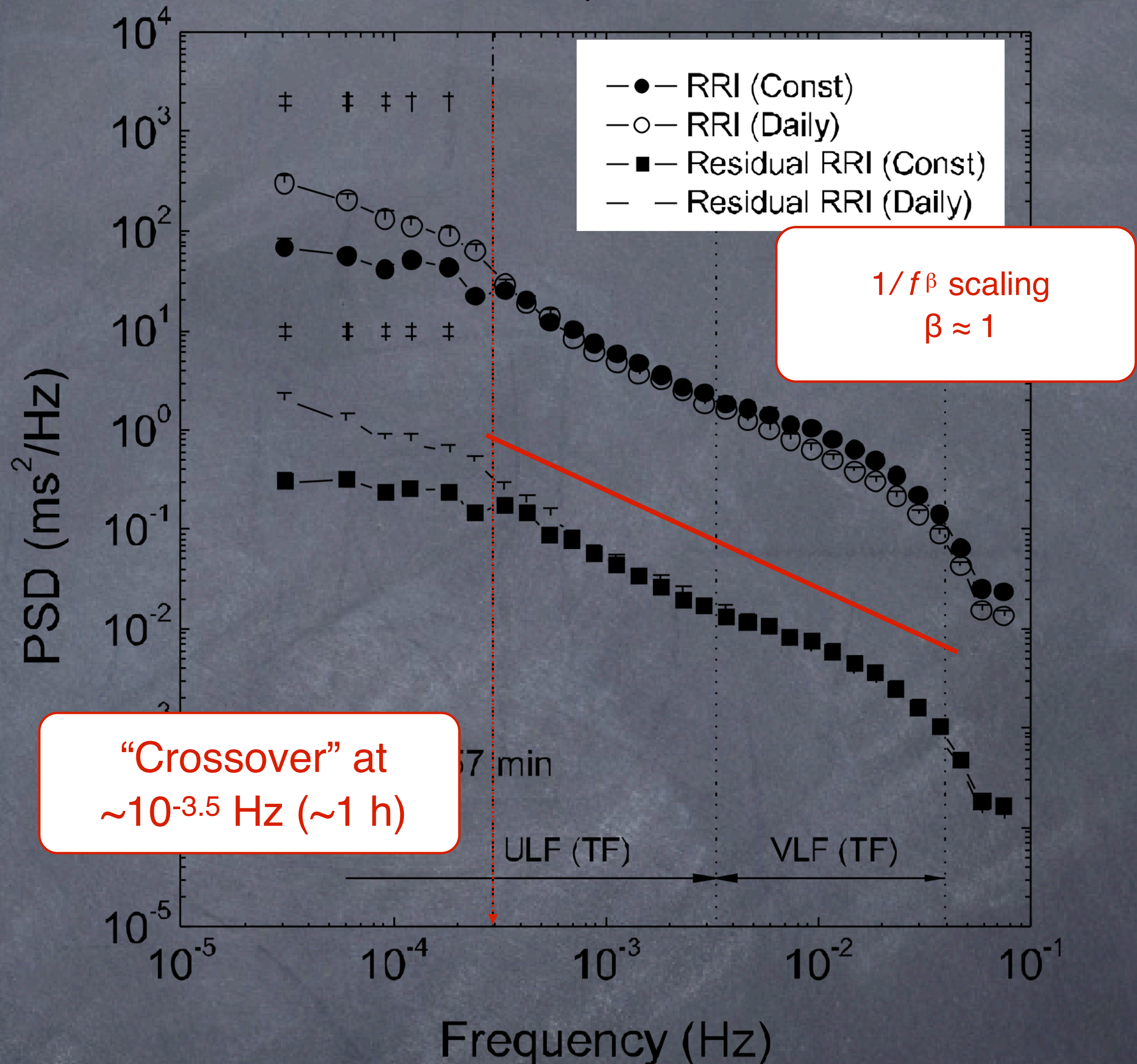
Electrocardiography (ECG)



RR intervals



Power Spectrum



Comparison between quiescent and usual daily activity conditions (†)

Behavioral-independent from a few tenths to a few thousands of heartbeats

[Aoyagi, et al., Am. J. Physiol. 285: R171, 2003]

Human heart rate as a benchmark of biological complexity

Characteristics of Healthy Human Heart Rate

- **$1/f^{\beta}$ scaling of power spectrum (long-range temporal auto-correlations)**
  [M. Kobayashi and T. Musha, IEEE Trans Biomed Eng **29**, 456 (1982)]
- **Multifractal scaling properties**
  [P. Ch. Ivanov *et al.*, Nature **399**, 461 (1999)]
- **Non-Gaussian probability density function in the increments**
  [C.-K. Peng *et al.*, Phys. Rev. Lett. **70**, 1343 (1993)]
- **Scale-invariant properties of non-Gaussian increment probability density function**
  [K. Kiyono *et al.*, Phys. Rev. Lett. **93** (2004) 178103]

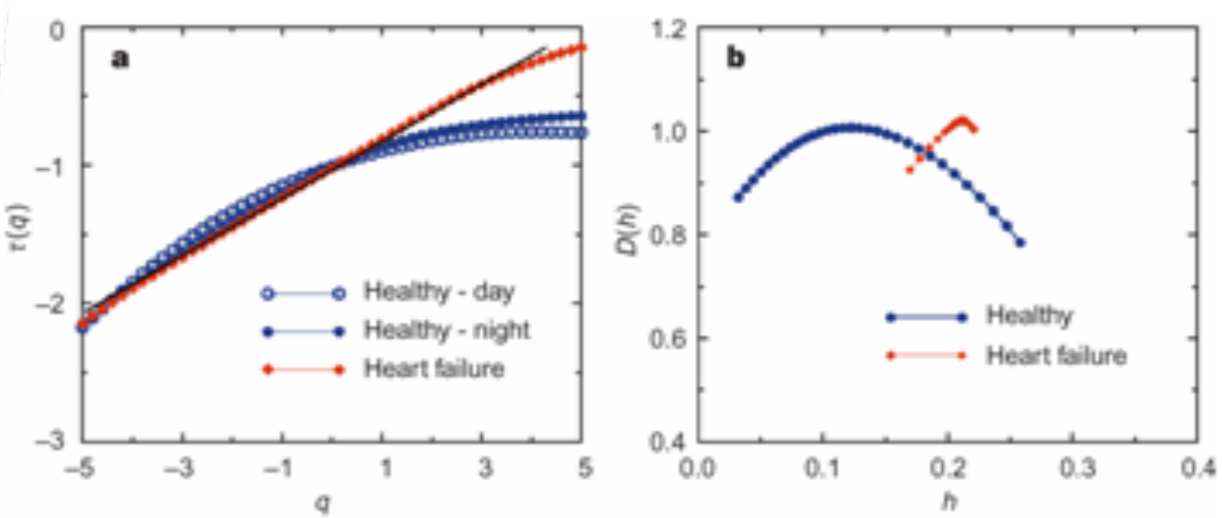
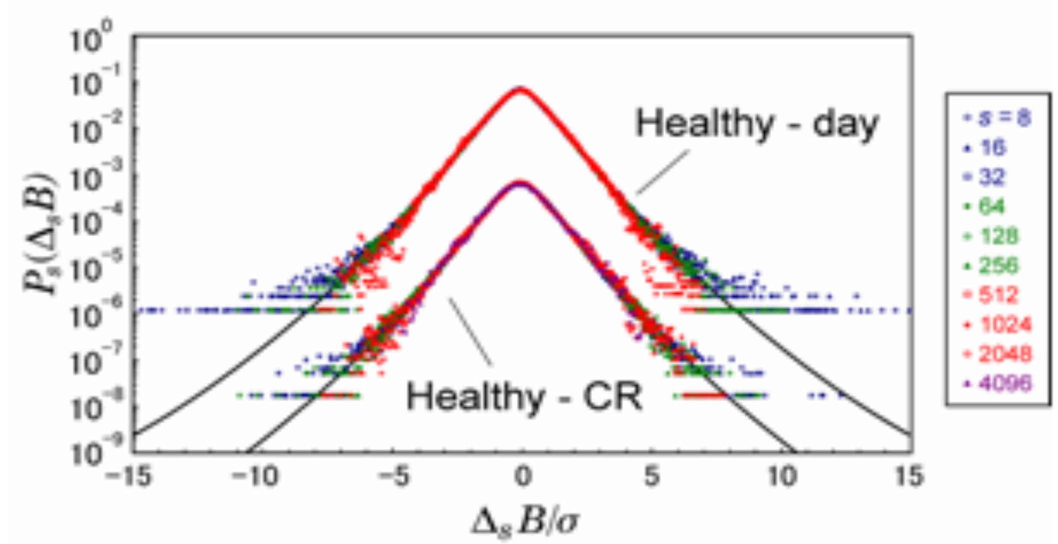
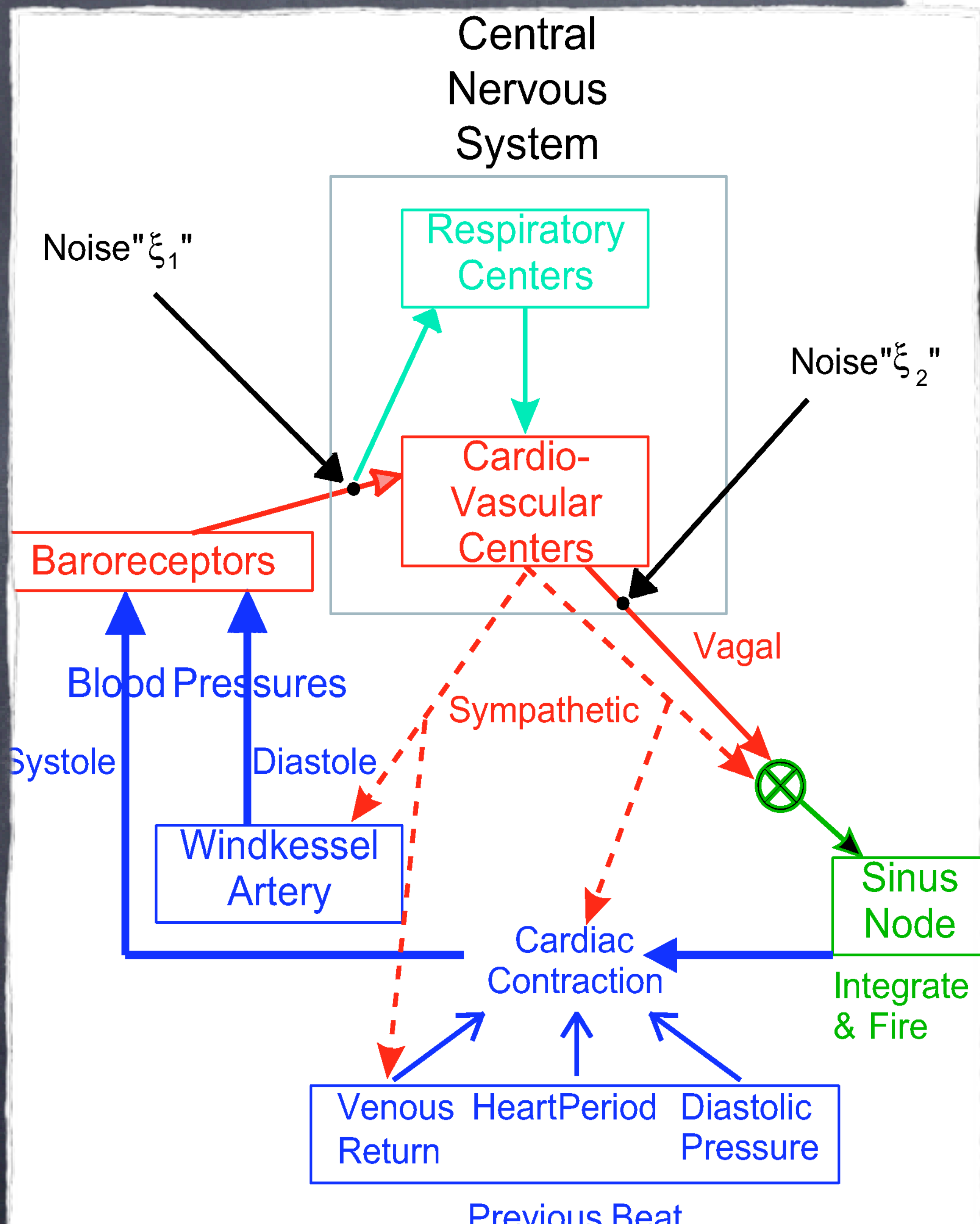
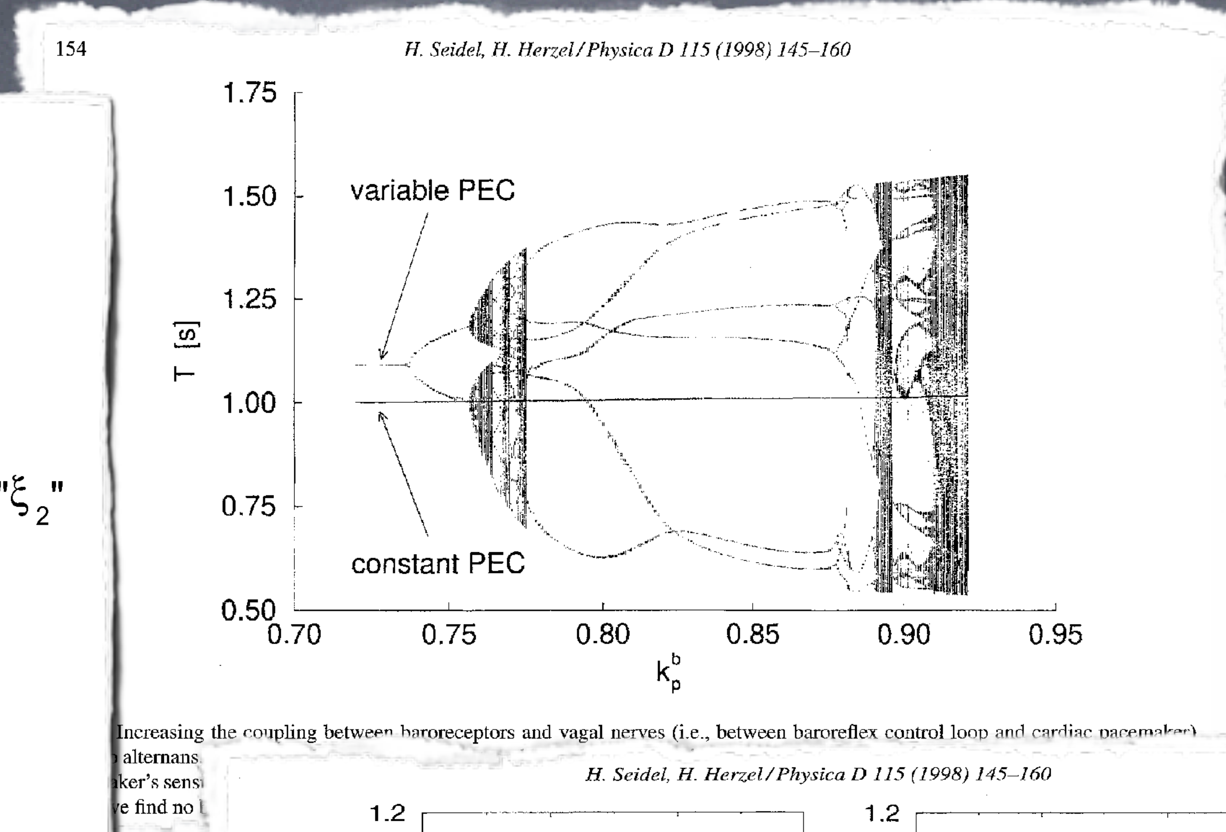


Figure 3 Multifractality in healthy dynamics. **a**, Multifractal spectrum $\tau(q)$ of the group averages for daytime and night-time records for 18 healthy subjects and 12 patients with congestive heart failure. The results show multifractal behaviour for the healthy group and different behaviour for the heart-failure group. **b**, Fractal dimensions $D(h)$ obtained through a Legendre transform from the group-averaged $\tau(q)$ spectra of **a**. The shape of $D(h)$ for the individual records and for the group average is broad, indicating multifractal behaviour. $D(h)$ for the heart-failure group is very narrow, indicating monofractality. The different form of $D(h)$ for the heart-failure group may reflect perturbation of the cardiac neuroautonomic control mechanisms associated with this pathology.



All complex characteristics confirmed in the heart control model: Kotani et al PRE 2005





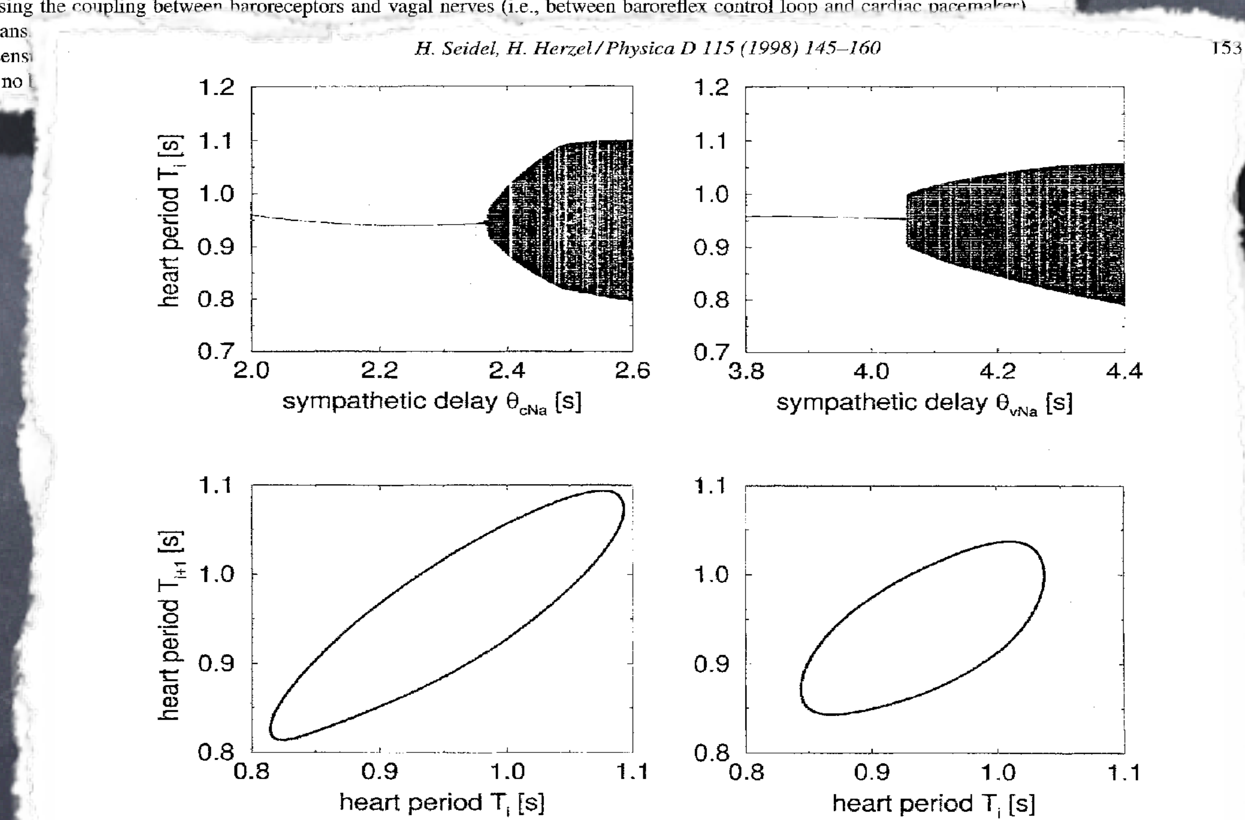


Fig. 5. Bifurcation to heart rate oscillations induced by a prolongation of the time delay of sympathetic activity between brain and (a) heart or (b) blood vessels. Characteristic return maps of these oscillations are depicted for (c) θ_{cNa} ... (d) $\theta_{vNa} = 4.2$ s

C.-K. Peng, J. Mietus, J.M. Hausdorff, S. Havlin, H.E. Stanley, A. L. Goldberger, Long-range anticorrelations and non-Gaussian behavior of the heartbeat, Phys. Rev. Lett., 70, pp1343, 1993.

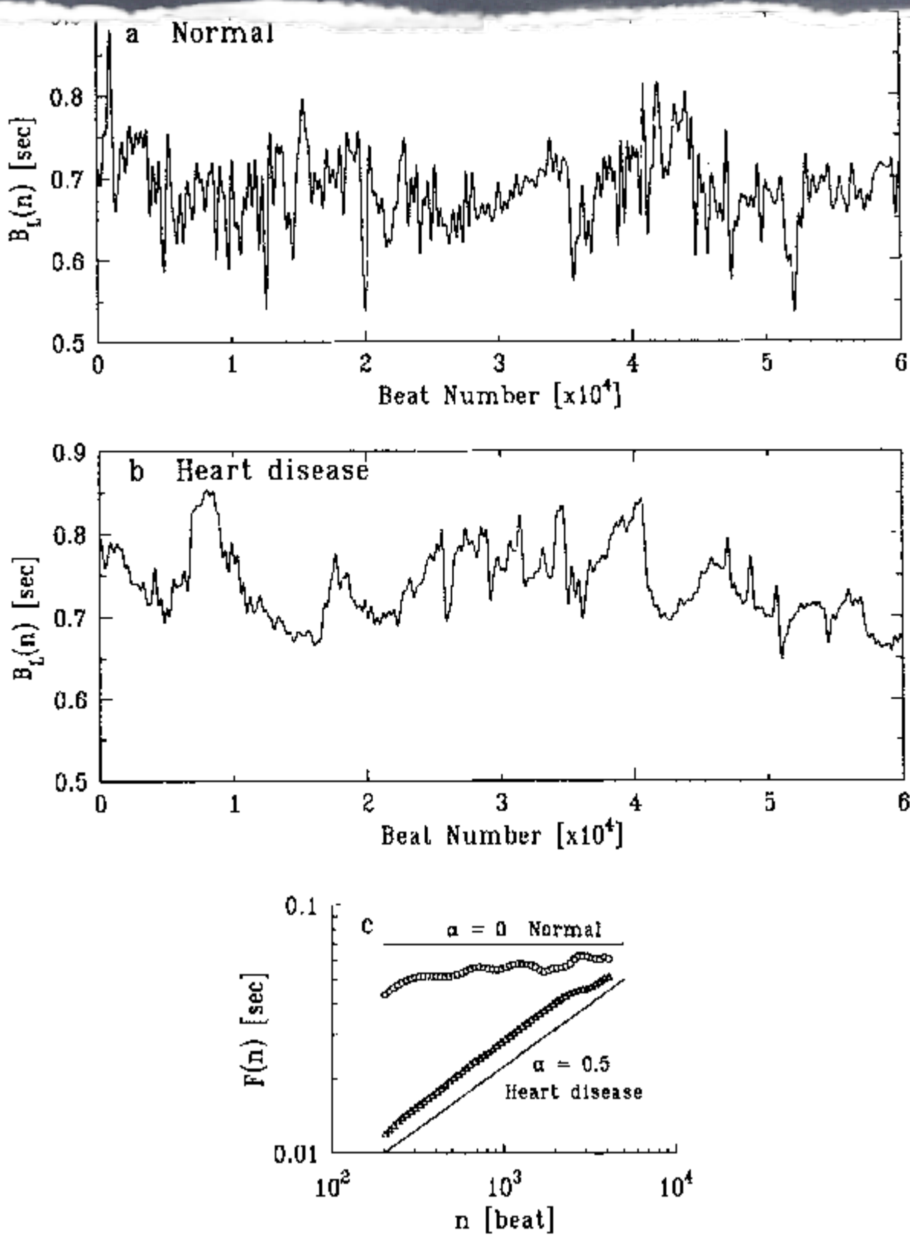


FIG. 1. The interbeat interval $B_L(n)$ after low-pass filtering for (a) a healthy subject and (b) a patient with severe cardiac disease (dilated cardiomyopathy). The healthy heartbeat time series shows more complex fluctuations compared to the diseased heart rate fluctuation pattern that is close to random walk ("Brownian") noise. (c) Log-log plot of $F(n)$ vs n. The circles represent $F(n)$ calculated from data in (a) and the triangles from data in (b). The two best-fit lines have slope $\alpha = 0.07$ and $\alpha = 0.49$ (fit from 200 to 4000 beats). The two lines with slopes $\alpha = 0$ and $\alpha = 0.5$ correspond to "$1/f$ noise" and "Brownian noise," respectively. We observe that $F(n)$ saturates for large n (of the order of 5000 beats), because the heartbeat intervals are subjected to physiological constraints that cannot be arbitrarily large or small. The low-pass filter removes all Fourier components for $f \geq f_c$. The results shown here correspond to $f_c = 0.005$ beat^{-1}, but similar findings are obtained for other choices of $f_c \leq 0.005$. This cutoff frequency f_c is selected to remove components of heart rate variability associated with physiologic respiration or pathologic Cheyne-Stokes breathing as well as oscillations associated with baroreflex activation (Mayer waves).

VOLUME 70, NUMBER 9 PHYSICAL REVIEW LETTERS 1 MARCH 1993

C.-K. Peng, J. Mietus, J.M. Hausdorff, S. Havlin, H.E. Stanley, A. L. Goldberger, Long-range anticorrelations and non-Gaussian behavior of the heartbeat, Phys. Rev. Lett., 70, pp1343, 1993.

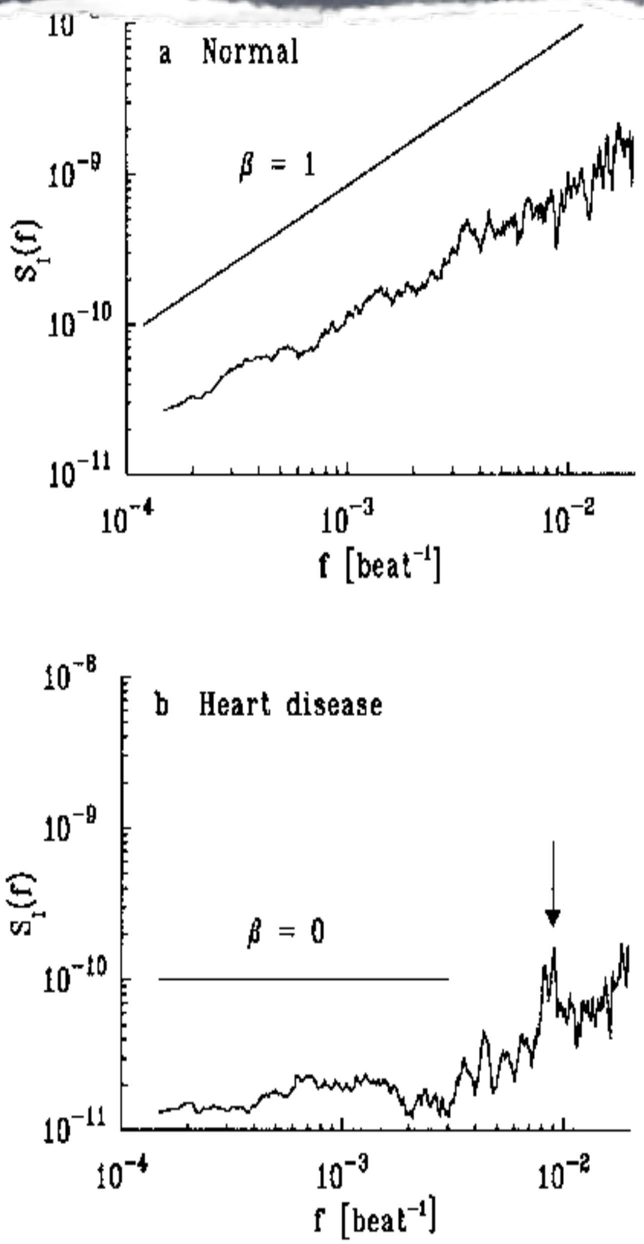


FIG. 3. The power spectrum $S_I(f)$ for the interbeat interval increment sequences over $\sim$ 24 h for the same subjects in Fig. 1. (a) Data from a healthy adult. The best-fit line for the low-frequency region has a slope $\beta = 0.93$. The heart rate spectrum is plotted as a function of "inverse beat number" (beat^{-1}) rather than frequency (time^{-1}) to obviate the need to interpolate data points. The spectral data are smoothed by averaging over fifty values. (b) Data from a patient with severe heart failure. The best-fit line has slope 0.14 for the low-frequency region, $f < f_c = 0.005$ beat^{-1}. The appearance of a pathologic, characteristic time scale is associated with a spectral peak (arrow) at about 10^{-2} beat^{-1} (corresponding to Cheyne-Stokes respiration).

M. Costa, A.L. Goldberger, C.-K. Peng, Multiscale Entropy Analysis of Complex Physiologic Time Series, Phys. Rev. Lett., 89, pp068102, 2002.

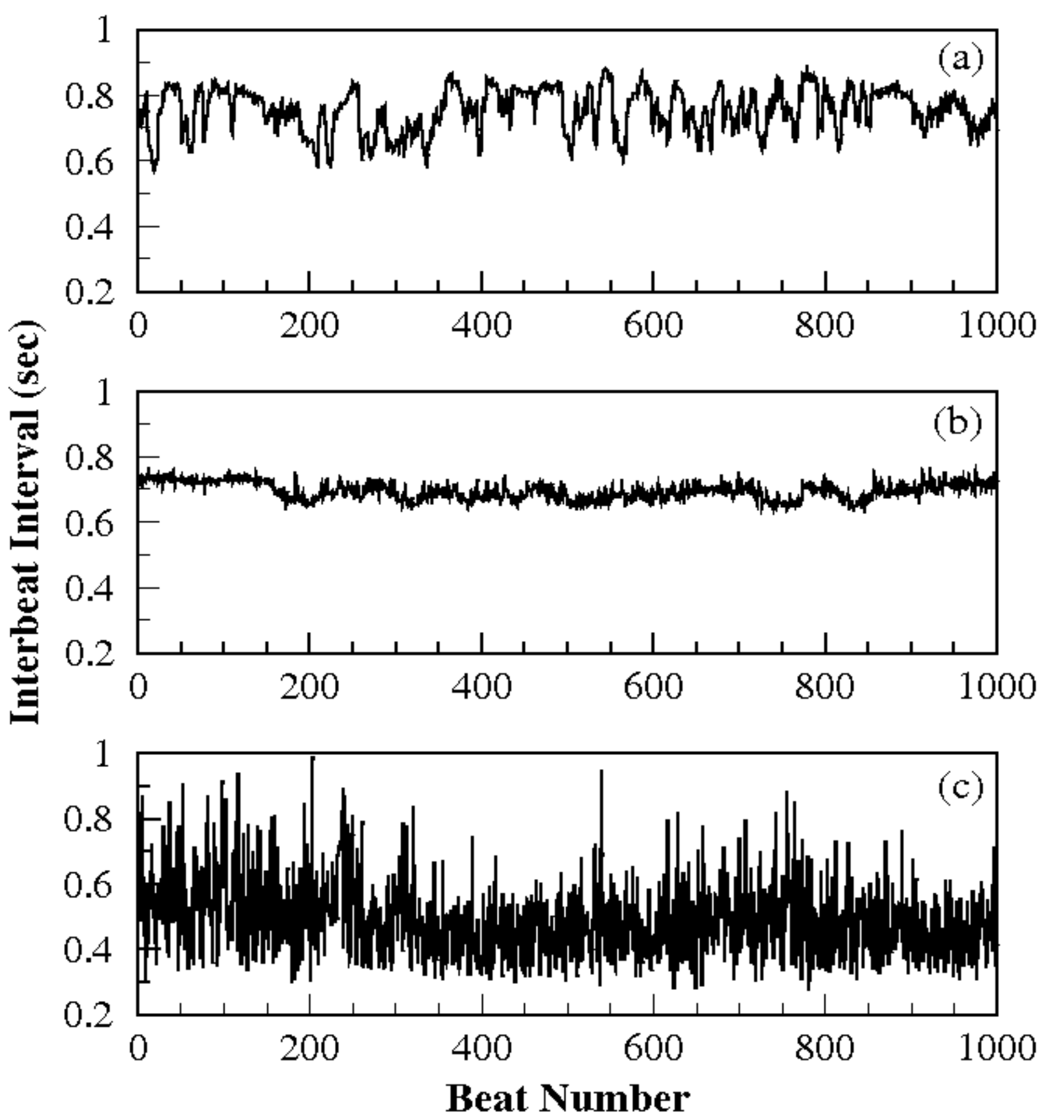


FIG. 2. Representative heartbeat intervals time series from (a) healthy individual (sinus rhythm), (b) subject with congestive heart failure (sinus rhythm), and (c) subject with the cardiac arrhythmia, atrial fibrillation.

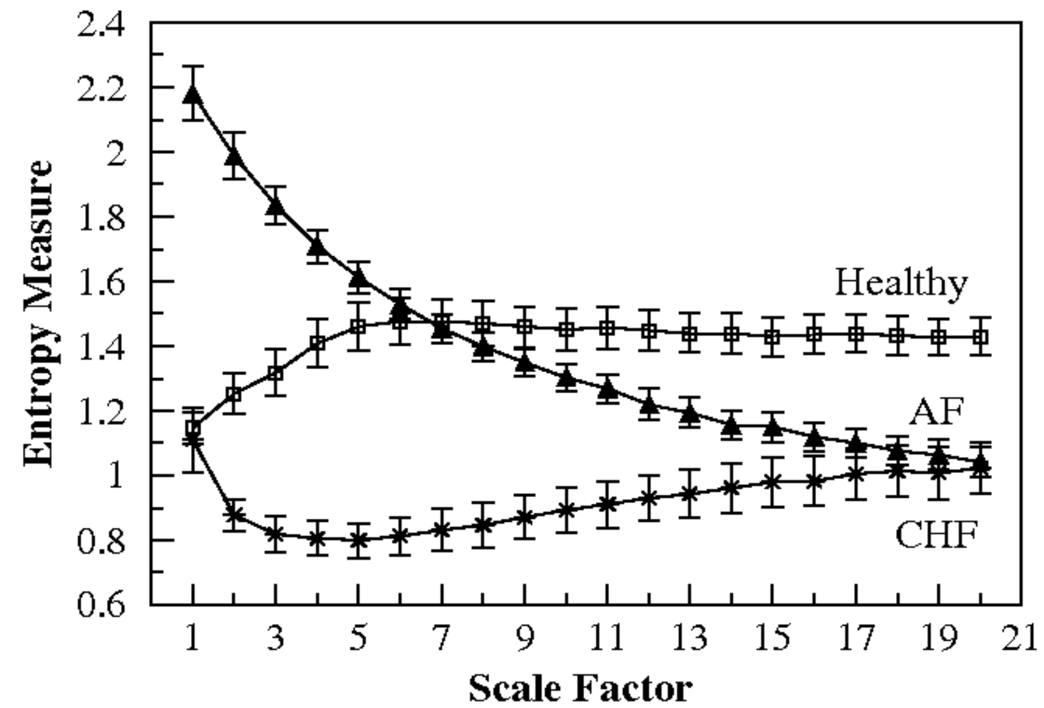


FIG. 3. MSE analysis of interbeat interval time series derived from healthy subjects, subjects with congestive heart failure (CHF), and subjects with atrial fibrillation (AF), as shown in Fig. 2. Values are given as means $\pm$ standard error [16]. Time series were filtered to remove outlier points due to artifacts and ventricular ectopic beats. The values of entropy depend on the scale factor. For scale one, AF time series are assigned the highest value of entropy, and the values corresponding to healthy and CHF groups completely overlap. For larger scales, e.g., 20, the entropy value for the coarse-grained time series derived from healthy subjects is significantly higher than those for AF and CHF. At this scale, AF and CHF groups become indistinguishable.

D.R. Chialvo, Physiology: Unhealthy surprises, Nature 419, pp263, 2002.

Unhealthy surprises

Dante R. Chialvo

Fluctuations in heart rate can signal disease and may prove fatal. A measurement, based on entropy, of how 'surprising' the beat irregularity is, distinguishes healthy hearts from those suffering common forms of illness.

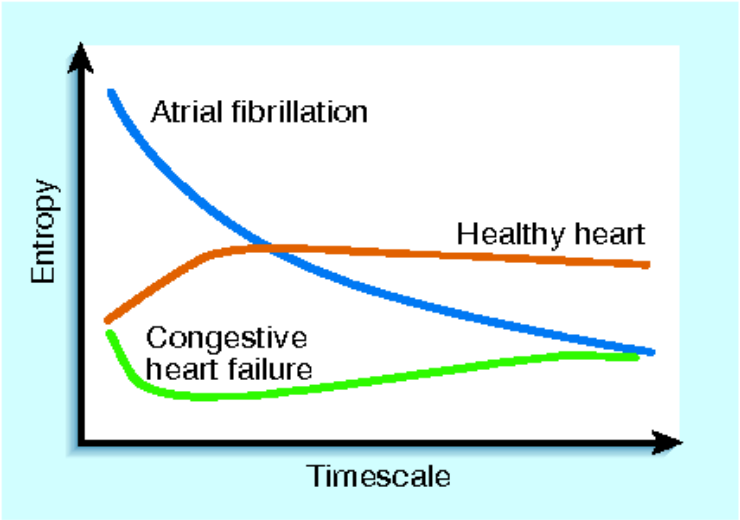
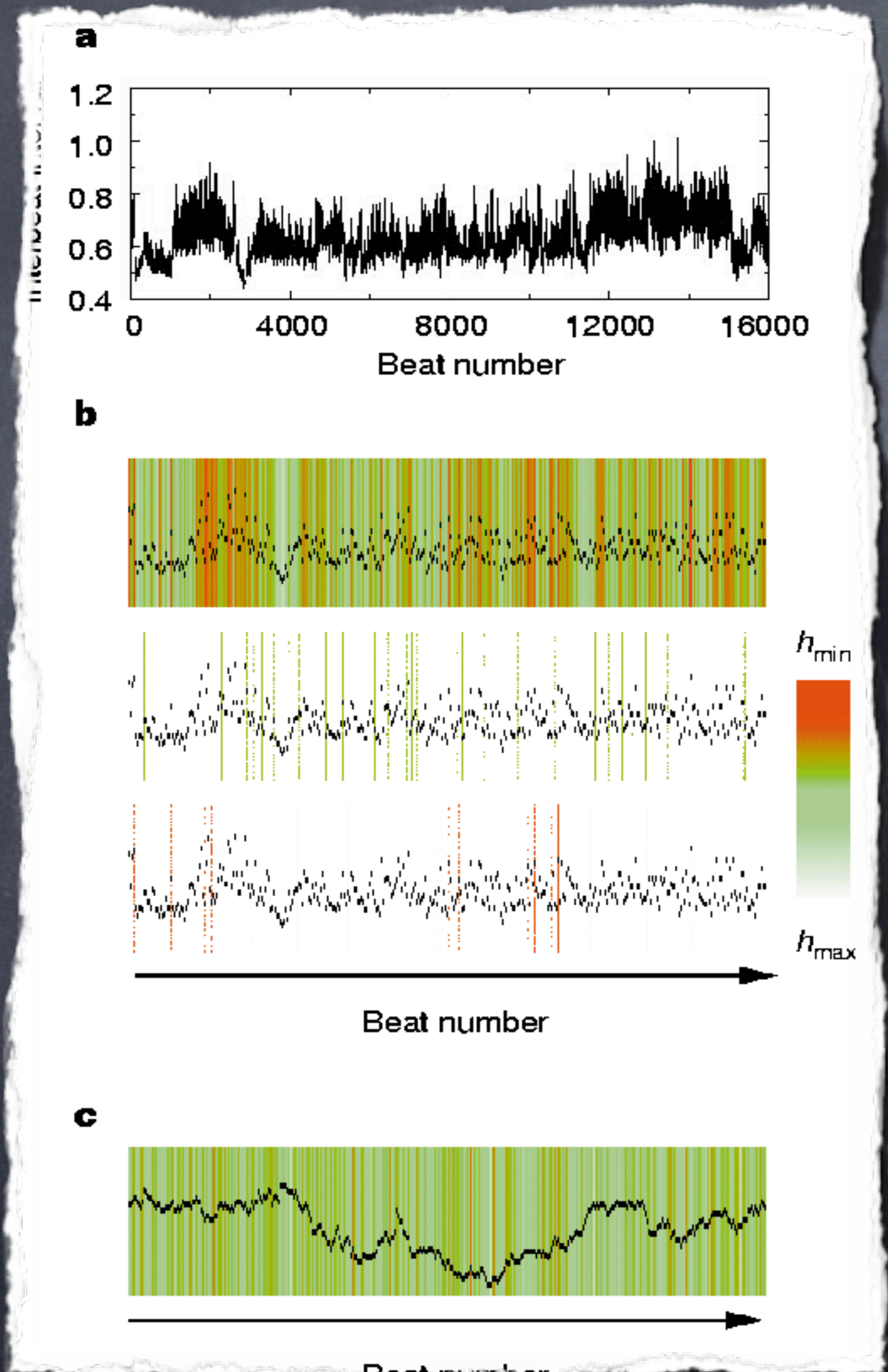
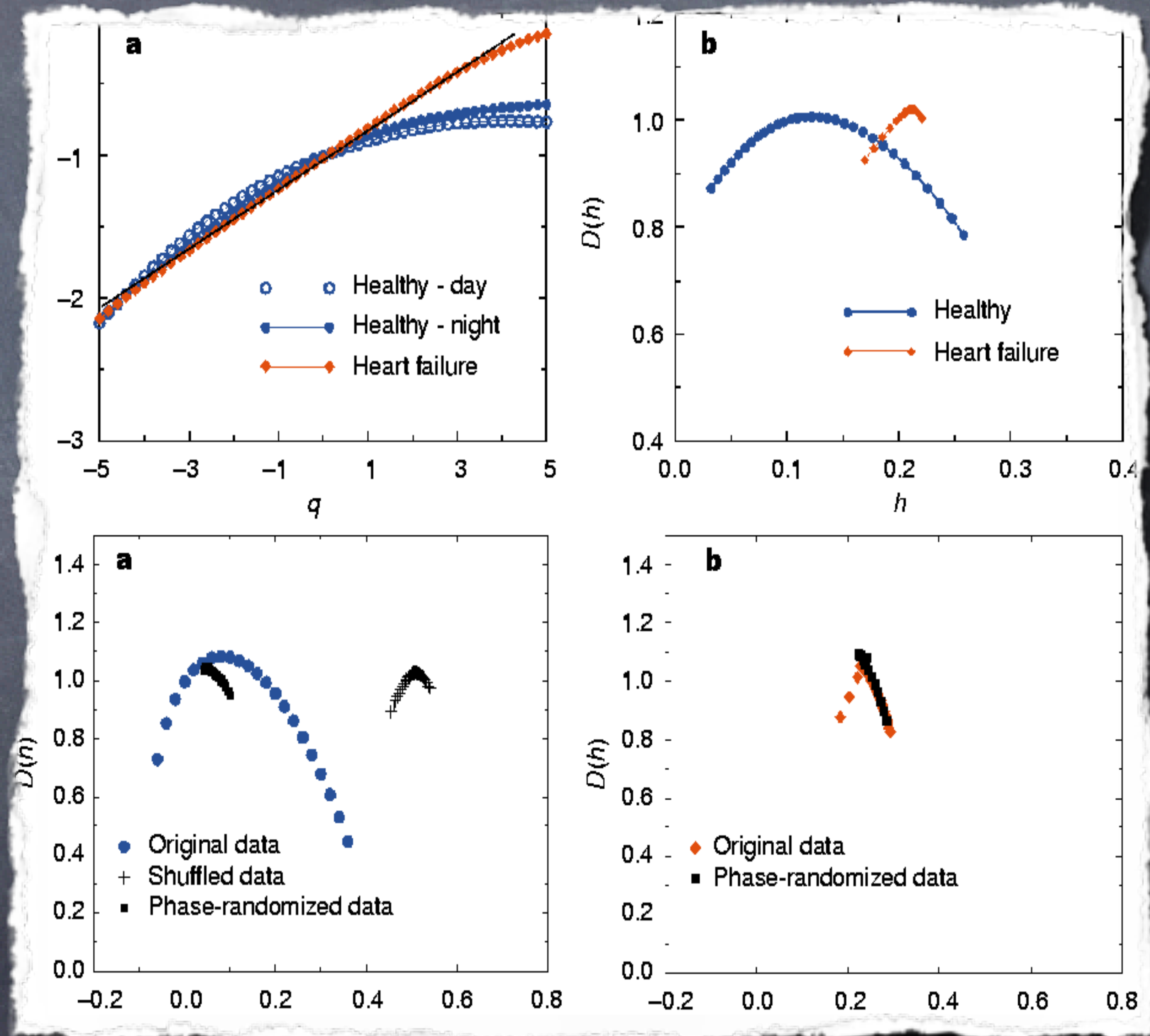


Figure 1 **Entropy and the healthy heart. By analysing the entropy, or disorder, of the intervals between heart beats on different timescales, Costa *et al.*[2] show that the entropy curve distinguishes the behaviour of a healthy heart from that of an unhealthy heart, for example one suffering from atrial fibrillation or congestive heart failure.**

P.Ch. Ivanov, L.A.N. Amaral, A.L. Goldberger, S. Havlin, M.G. Rosenblum, Z.R. Struzik, H.E. Stanley, Multifractality in human heartbeat dynamics, Nature 399, pp461, 1999.





The Problem:

Reduced variability and complexity of human heart rate in severe heart disease, including congestive heart failure (CHF), has become one of the key yardsticks by which new complexity measures are validated.

Consideration of reduced variability in severe heart disease has become one of the recommendations for the interpretation of HRV by the influential standardizing work [TaskForce, 1996], now registering 1,500 citations.

Indeed, there is an emergent belief that the lower variability and lower complexity of heart rate observed in CHF are associated with a higher risk of mortality.

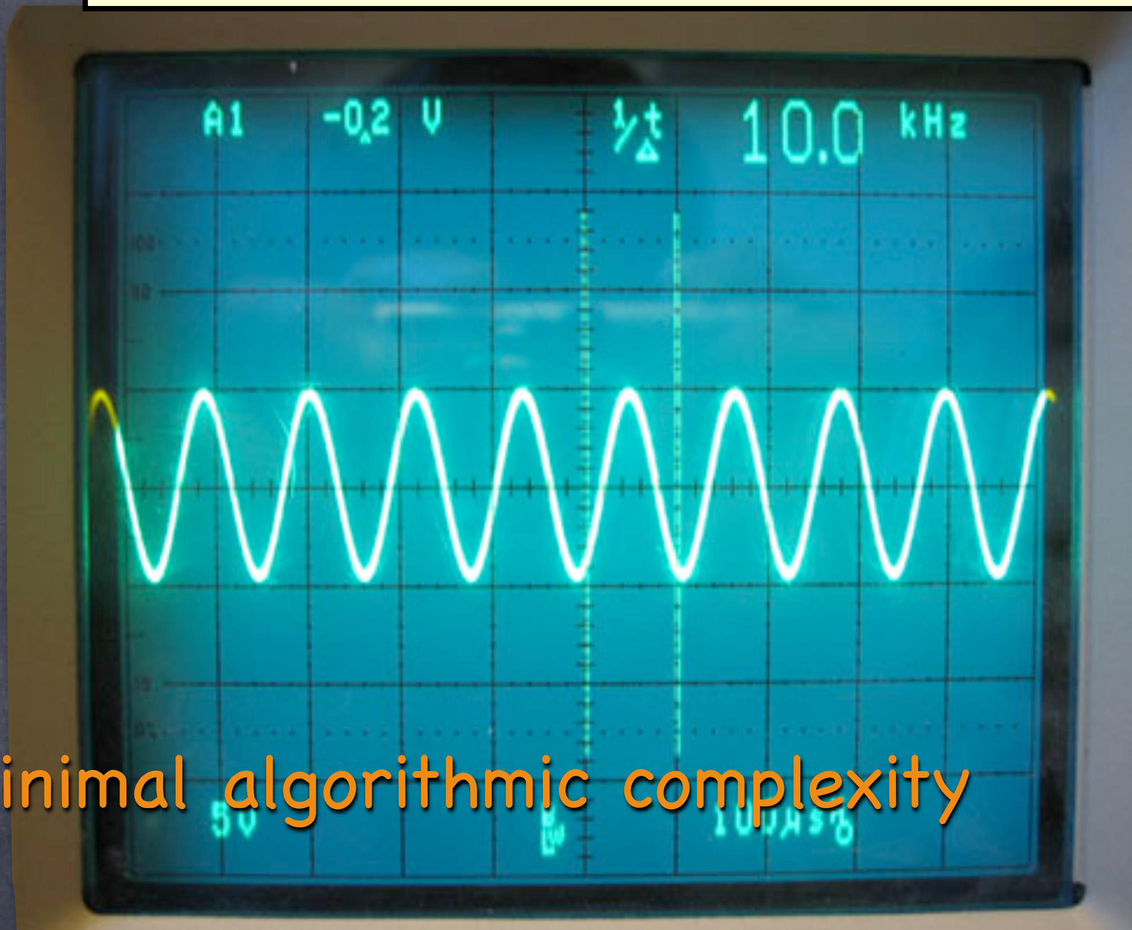
Yet, the focus of attention of the past research on HRV complexity in CHF has been limited to CHF diagnosis from HRV.

Why analyse fluctuations?

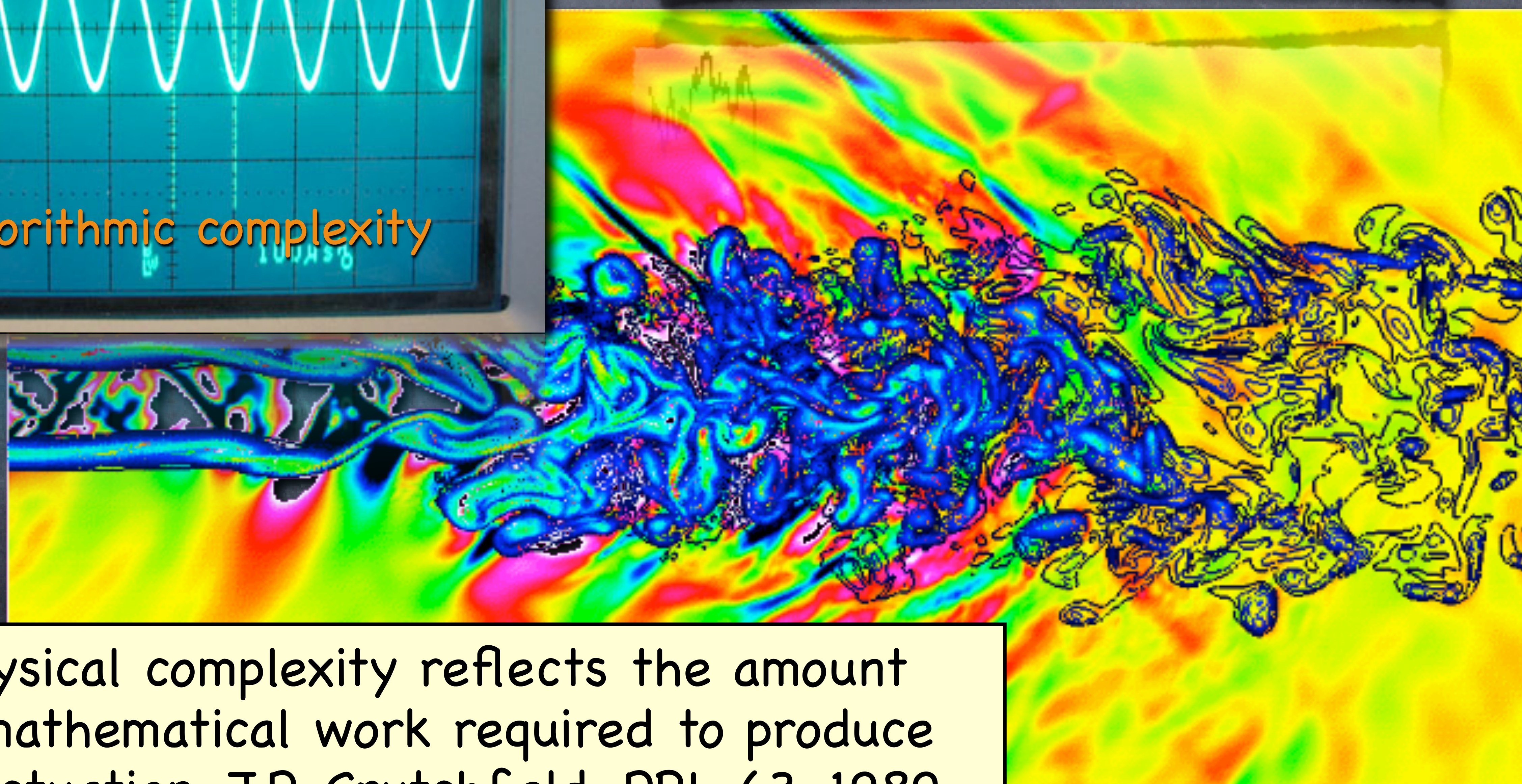
Lowest physical complexity

Maximal algorithmic complexity

Lowest physical complexity

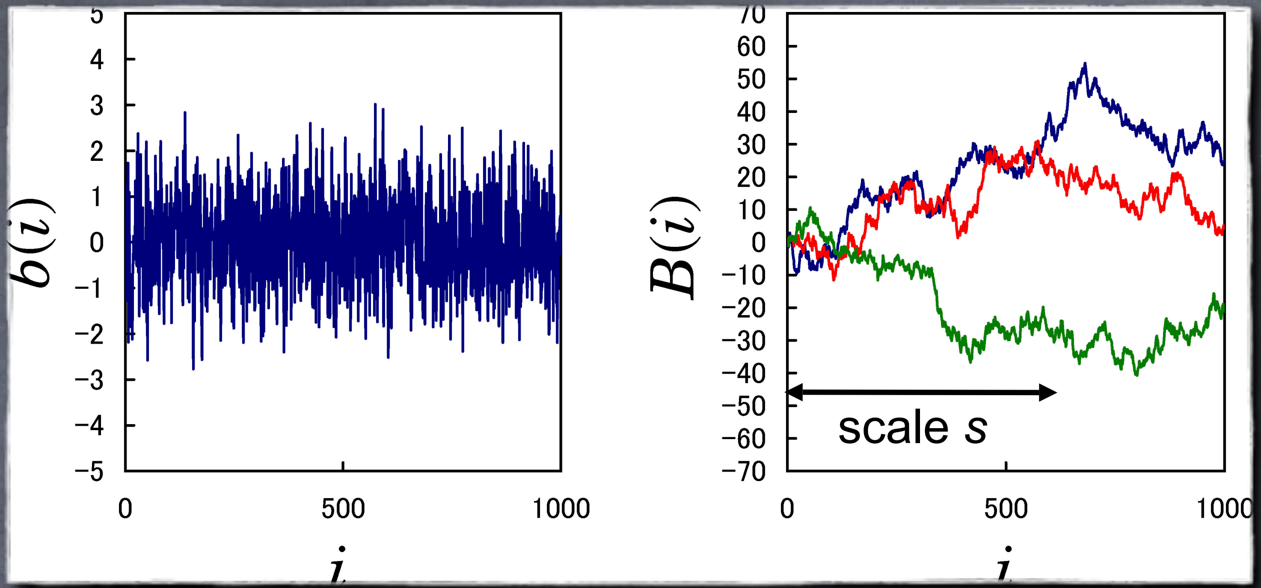


Minimal algorithmic complexity



Physical complexity reflects the amount of mathematical work required to produce a fluctuation, J.P. Crutchfield, PRL 63, 1989.

Multiscale Probability Density Function



Integrated series:

$$B(i) = \sum_{j=1}^{i} b(j)$$

Extension of Random Walk Method

Structure function analysis:

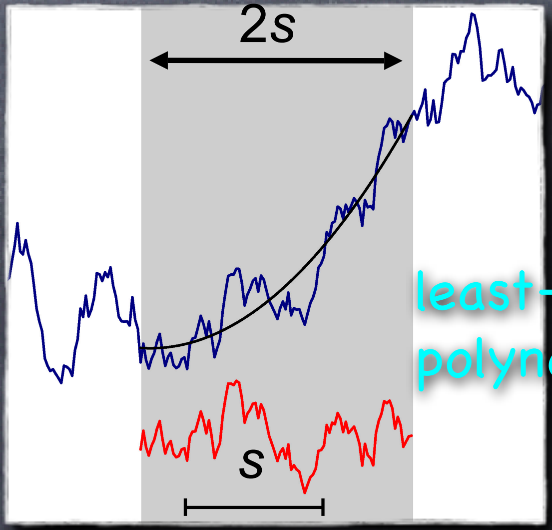
$$S(s) = E\left[\{B(i+s) - B(i)\}\right]$$

Multiscaling (multifractal) analysis

$$S_q(s) = E\left[\{B(i+s) - B(i)\}^q\right] \sim s^{\zeta(q)}$$

$$\text{monofractal}: \quad S_q(s) \sim s^{qH}$$

Scale-dependence of PDF of B(i+s) - B(i)

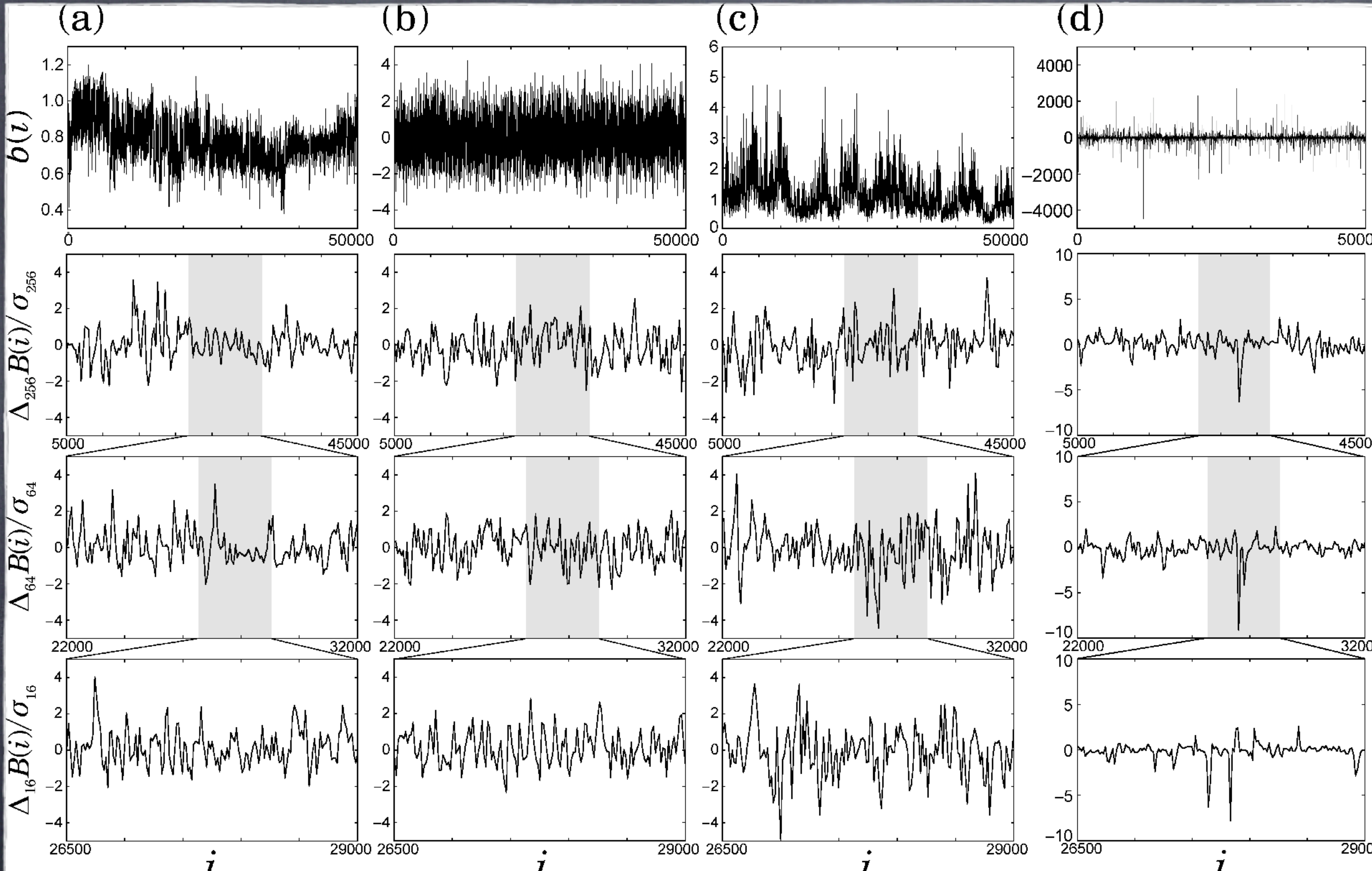


least-squares polynomial fit

After subtracting the local trend, we obtain the increment:

$D_sB(i)$ = {B(i+s) − (local trend)} − {B(i) − (local trend)}

All the time series below have the same statistics of sign change (Hurst exp)

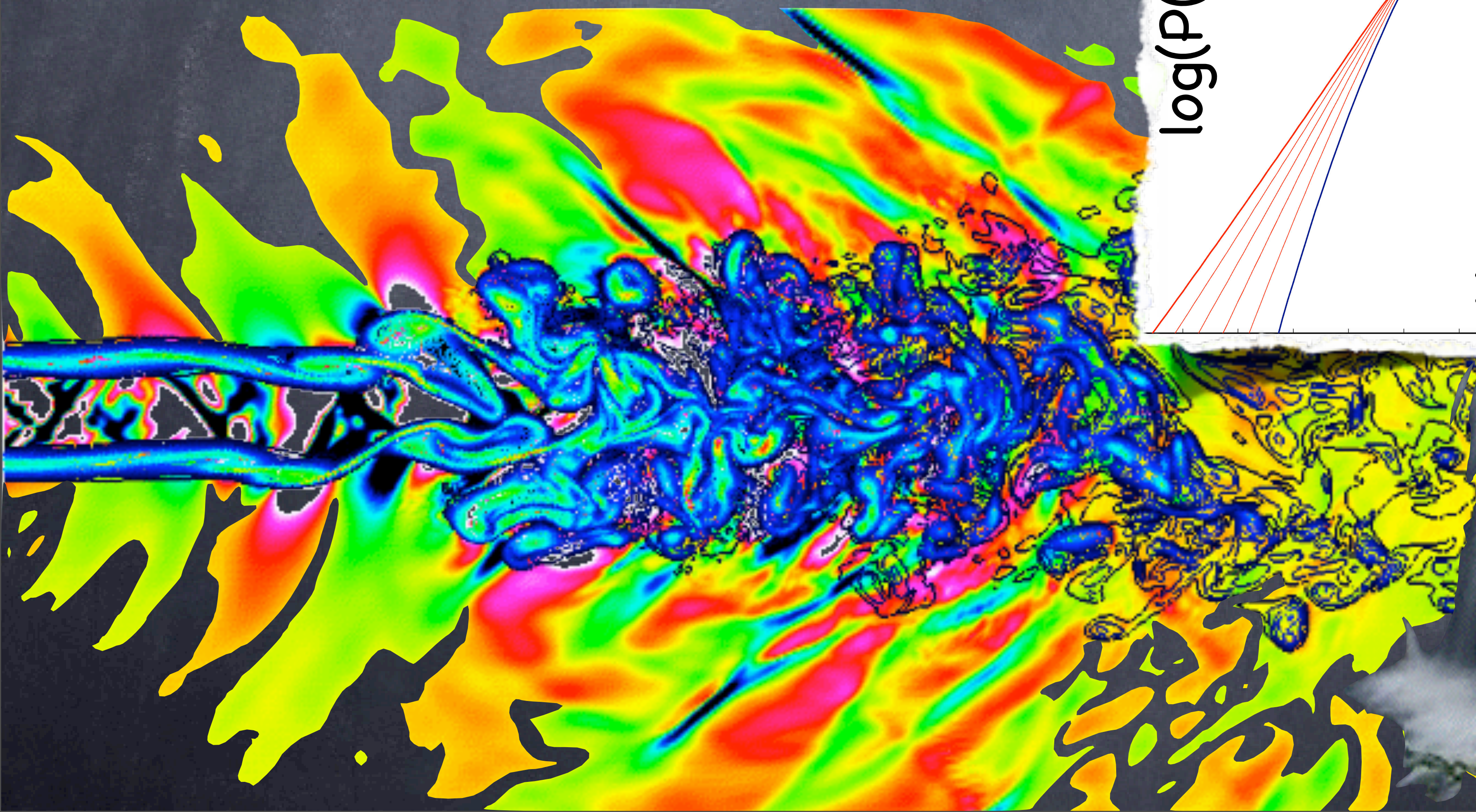


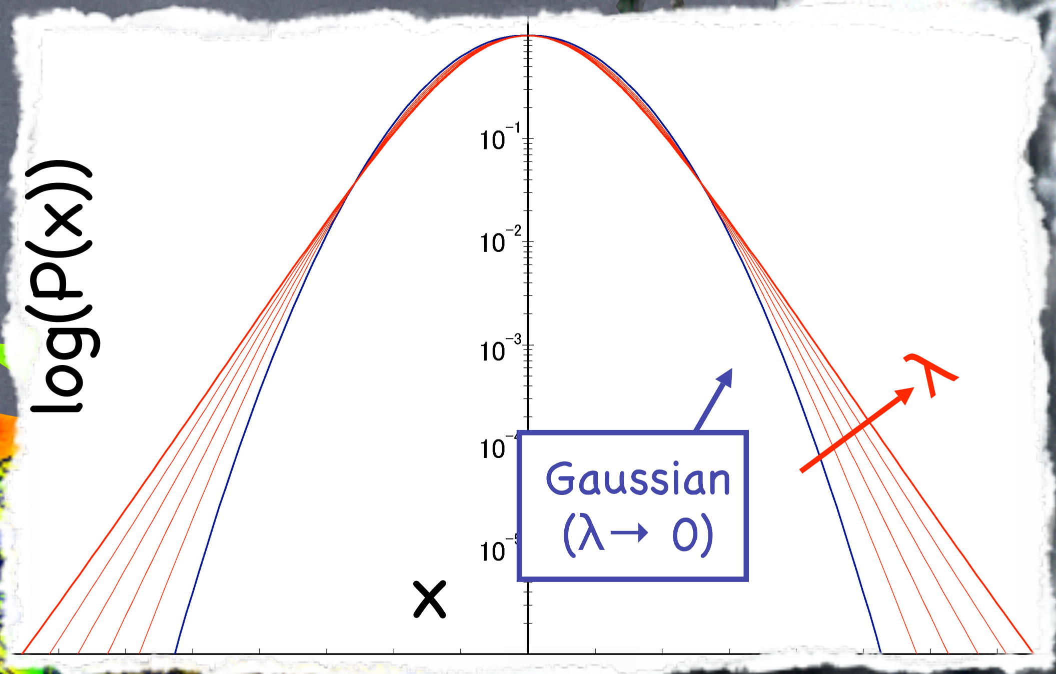
from Kiyono et al, *IEEE-Trans. Biomed. Eng.* **53**, 2006

PDF based on Castaing's equation (log-normal cascade)

[Castaing et al., Physica D 46 (1990) 177]

$$P(x) = \frac{1}{2\pi\lambda}\int_0^\infty \exp\left(-\frac{x^2}{2\sigma^2}\right)\exp\frac{(\log\sigma)^2}{2\underbrace{\lambda^2}_{\text{parameter}}}\frac{d\sigma}{\sigma^2}$$





"Multiscale Probability Density Function Analysis: Non-Gaussian and Scale-Invariant Fluctuations of Healthy Human Heartrate", Kiyono et al, IEEE-TBME 53, (2006)

$$\boxed{\Delta_s B(i) = \xi_s(i) e^{\omega_s(i)},}$$

where ξ_s and ω_s are random variables and independent of each other.

Multiplication of two random variables

(Gaussian) × (Log-normal)

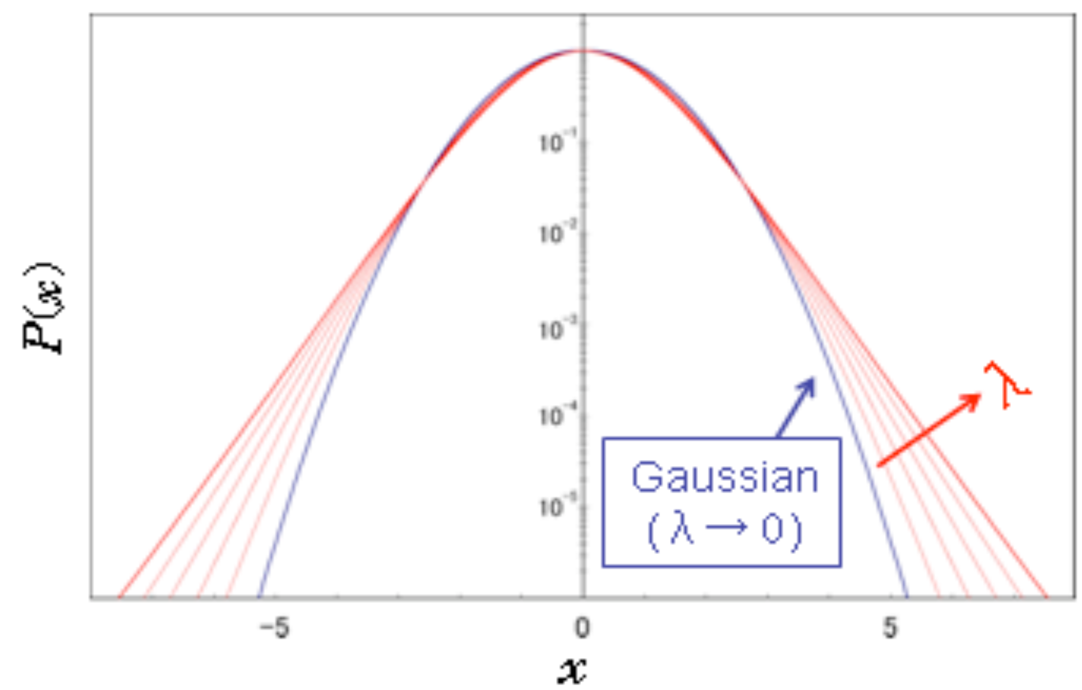
$$f(x)\mathrm{d}x = \frac{1}{\sqrt{2\pi}} \exp\left(-\frac{x^2}{2}\right) \mathrm{d}x$$

$$g(y)\mathrm{d}y = f(\log y)\,\mathrm{d}(\log y) = \frac{1}{\lambda\sqrt{2\pi}} \exp\left(-\frac{(\log y)^2}{2\lambda^2}\right) \mathrm{d}(\log y)$$

$$P(u)\mathrm{d}u = \int \frac{1}{\sqrt{2\pi}} \exp\left(-\frac{1}{2}\left(\frac{u}{x}\right)^2\right) \frac{1}{\lambda\sqrt{2\pi}} \exp\left(-\frac{(\log x)^2}{2\lambda^2}\right) \frac{\mathrm{d}(\log x)}{x} \mathrm{d}u = \left[\frac{1}{2\pi\lambda} \int \exp\left(-\frac{u^2}{2x^2}\right) \exp\left(-\frac{(\log x)^2}{2\lambda^2}\right) \frac{\mathrm{d}x}{x^2}\right] \mathrm{d}u$$

$$P(\Delta_s B) = \frac{1}{2\pi\lambda} \int_0^\infty \exp\left(-\frac{\Delta_s B^2}{2\sigma^2}\right) \exp\left(-\frac{(\log \sigma)^2}{2\underline{\lambda^2}}\right) \frac{\mathrm{d}\sigma}{\sigma^2}$$

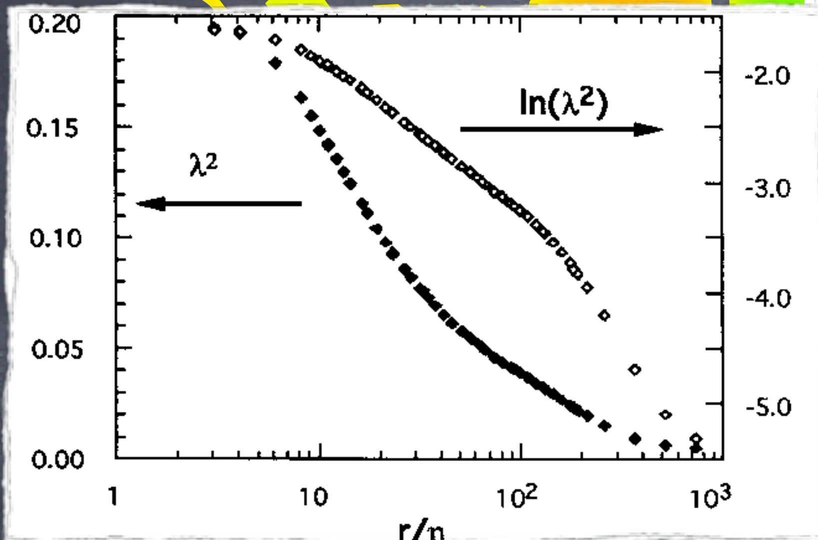
parameter

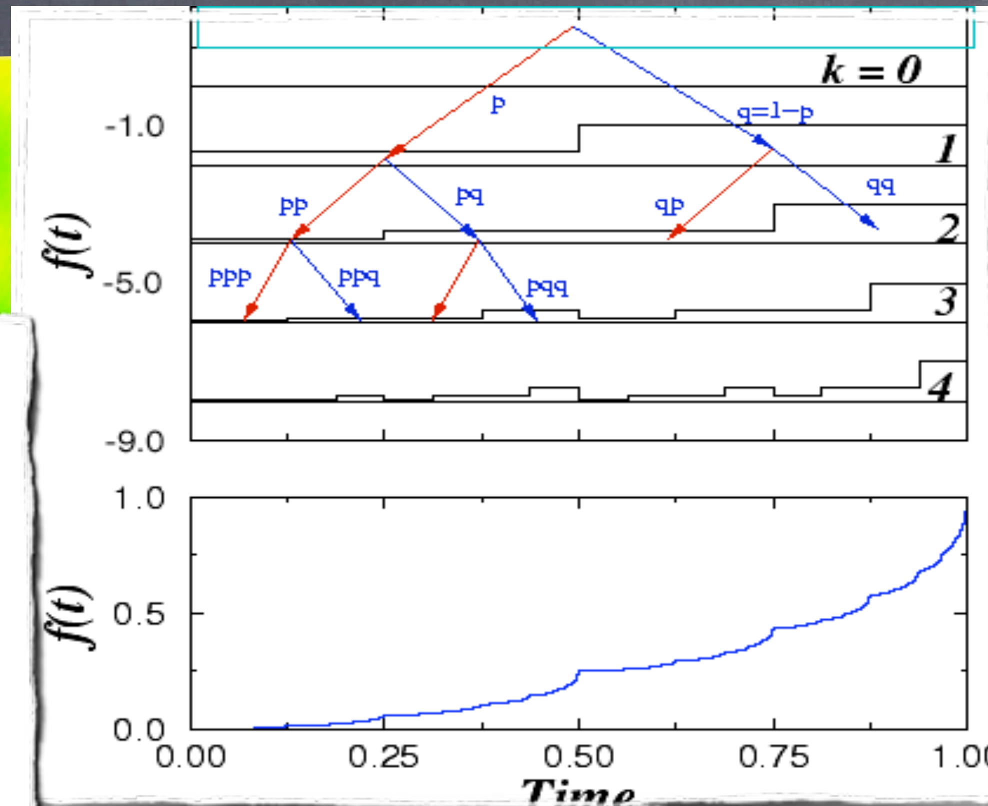


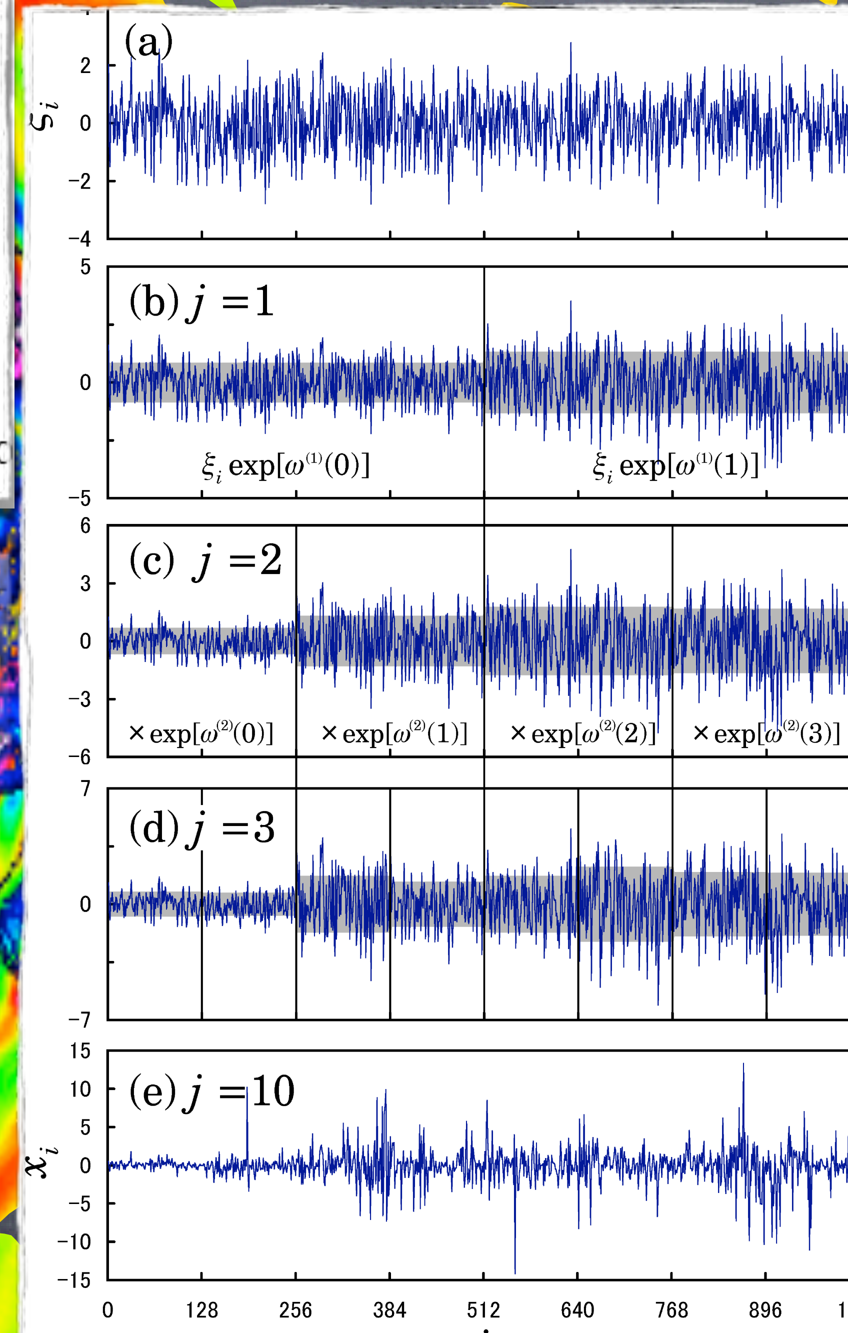
Parameter estimation of λ^2

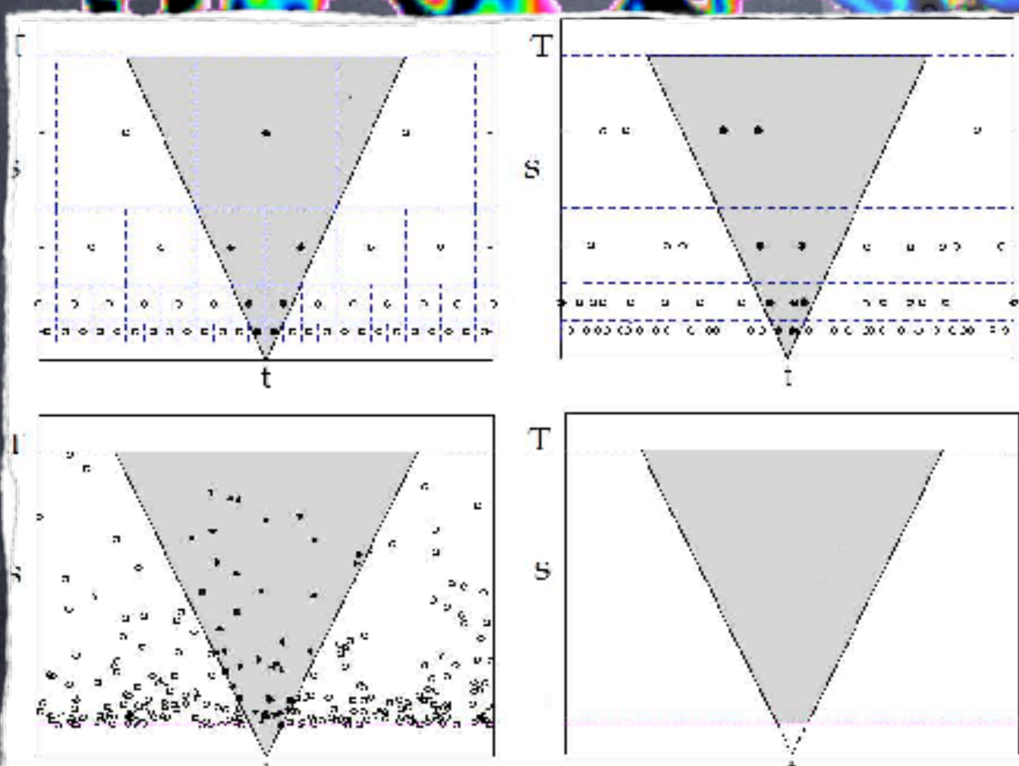
From discrete to continuous cascades

Chabaud et al PRL 73, 1994.









$$\theta_n(I_{k_1\ldots k_n}) = 2^{-n}\prod_{i=1}^{n} W_{k_1\ldots k_i} = 2^{-n} e^{\sum_{i=1}^{n}\delta\omega_{k_1\ldots}}$$

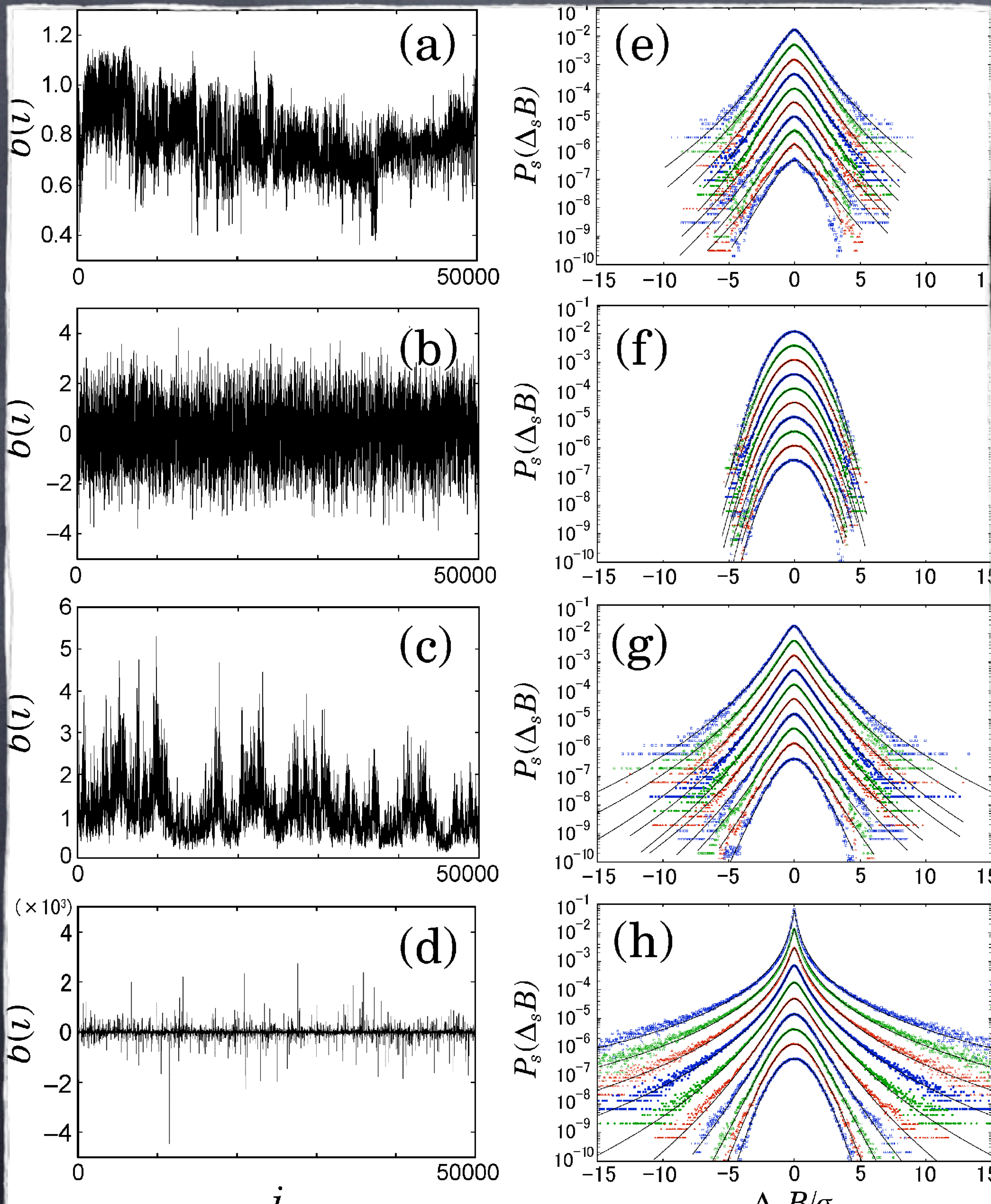
$$d\theta(t) = \prod_{(t_j,s_j)\in C(t)} W_j = e^{\sum_{(t_j,s_j)\in C(t)}\delta\omega_j}$$

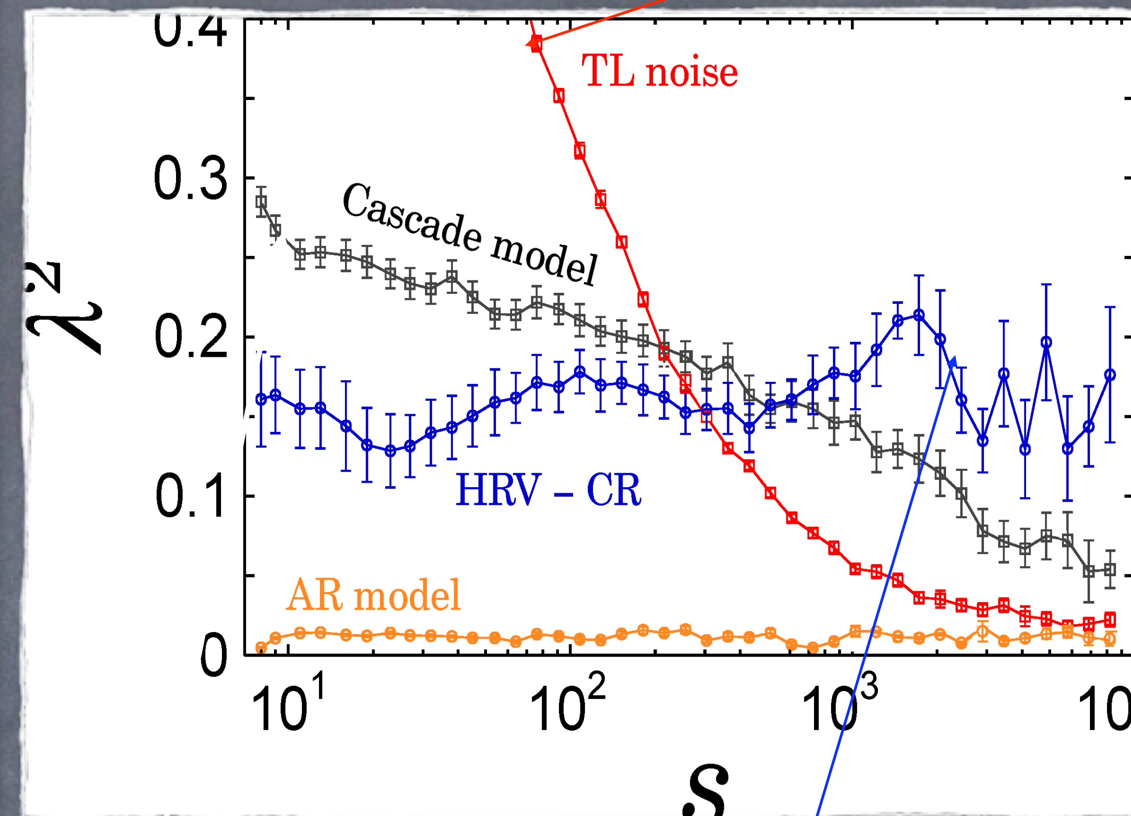
$$d\theta(t) = e^{\int_{(t',s)\in C(t)} d\omega(t',s)}$$

Bacry-Muzy construction

FIG. 1: **From discrete to continuous cascades:** (Top-Left) Mandelbrot Cascade lying on the dyadic tree. (Top-Right) "semi-continuous" Poisson construction obtained by "randomizing" the node positions at fixed scale. (Bottom-Left) Barral-Mandelbrot MPCP obtained by replacing the tree by a "random Poisson tree". (Bottom-Right) Log-infinitely divisible Bacry-Muzy construction.

Is multiscale PDF sufficient to characterise complexity?





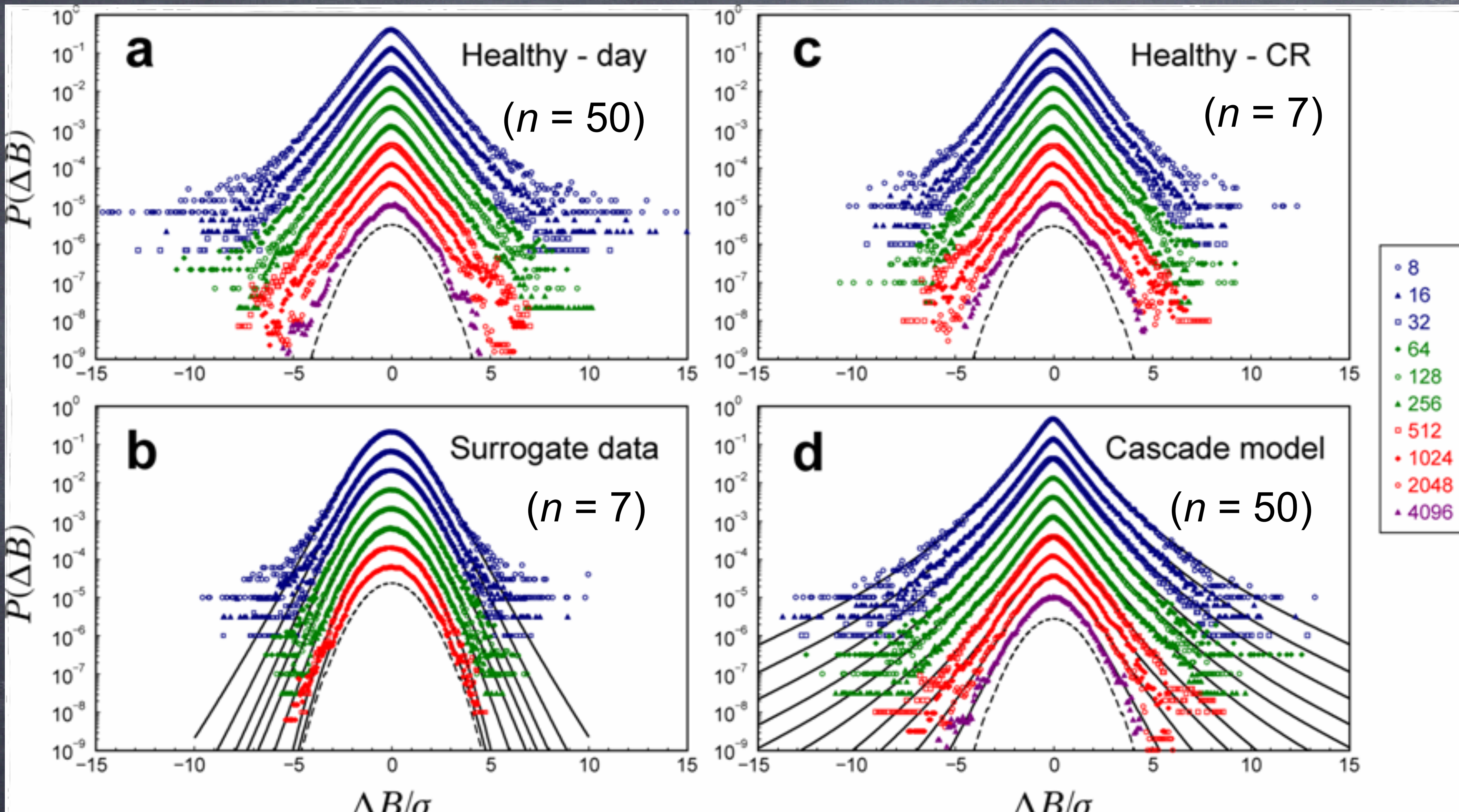
More complex?

cascade ~ log(s)

CLT violation?

Central Limit Theorem (IID)
s^(0.5) convergence speed -
Berry-Esseen theorem
W.Feller book Vol. 2.

Multiscale PDFs of healthy human HRV in daily activity and constant routine

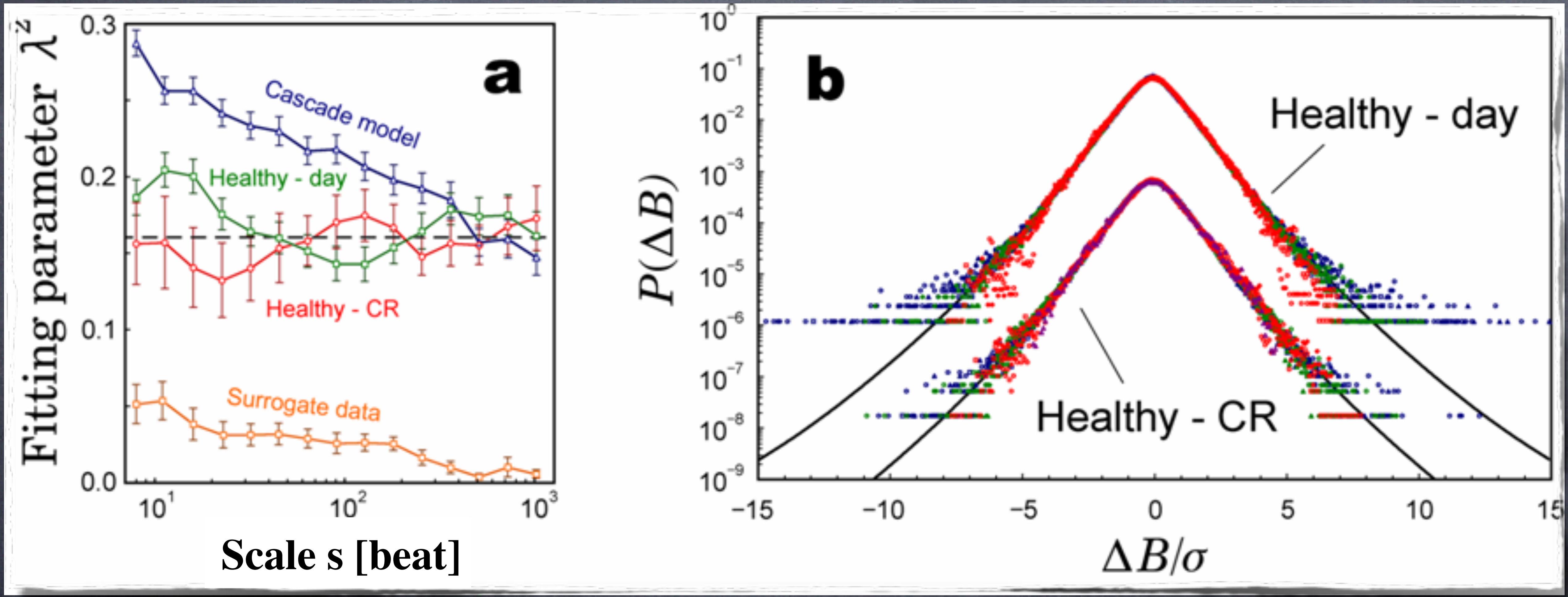


※ The dashed line is a Gaussian PDF for comparison

Scale-independence in the probability density function of healthy heart rate - K. Kiyono et al, PRL 93, 2004.

Scale-dependence of PDF

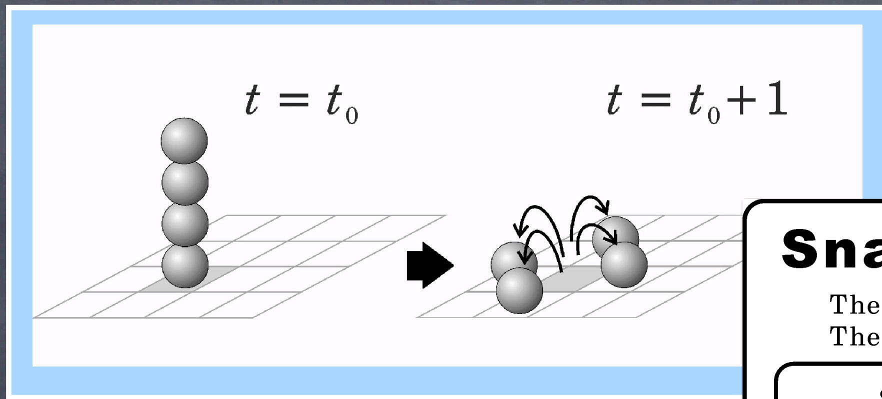
Collapse of the PDFs



※ "$\lambda^2 \to 0$" means convergence to a Gaussian

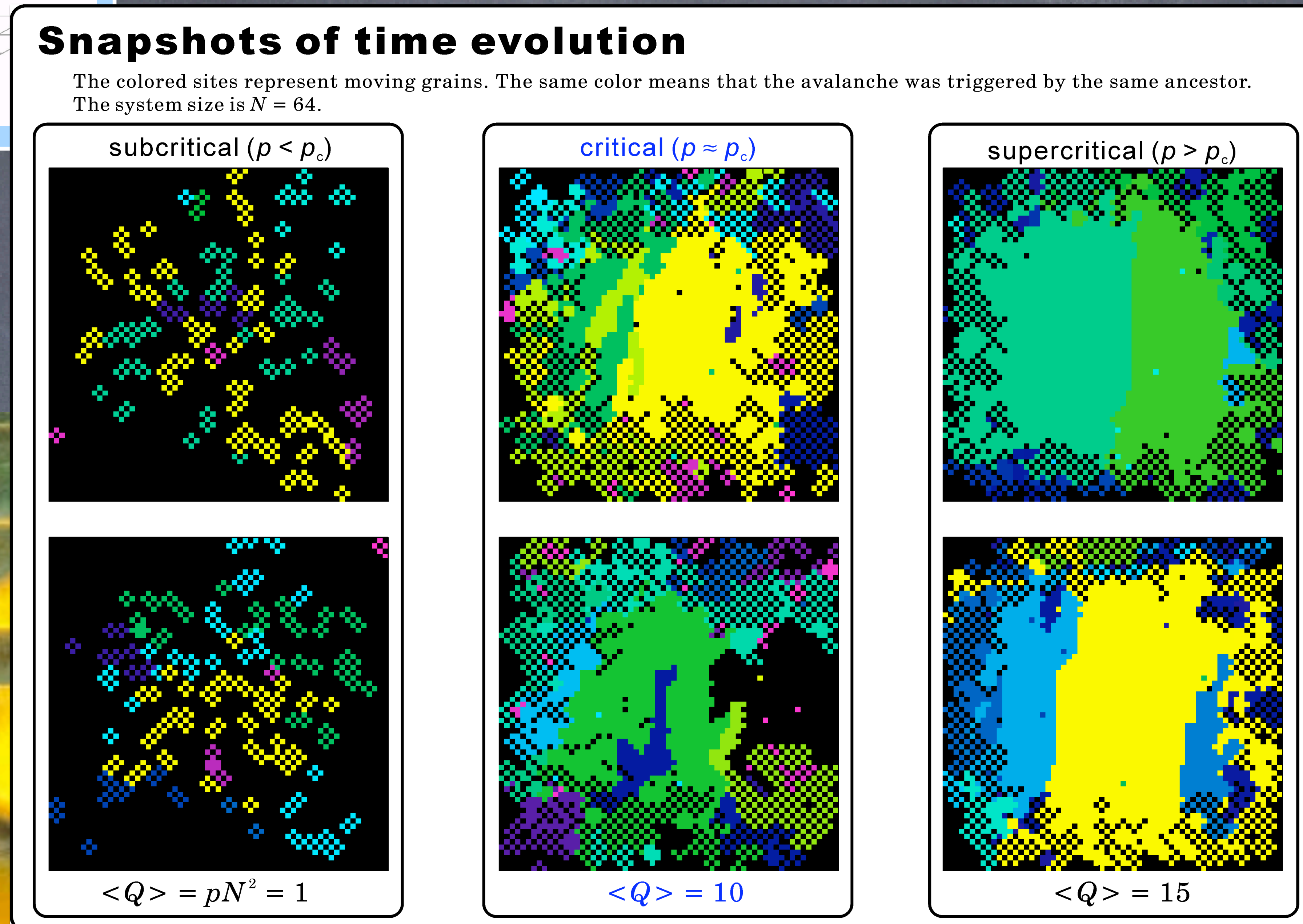
※ Random cascade process: $\lambda^2 \sim \log s$

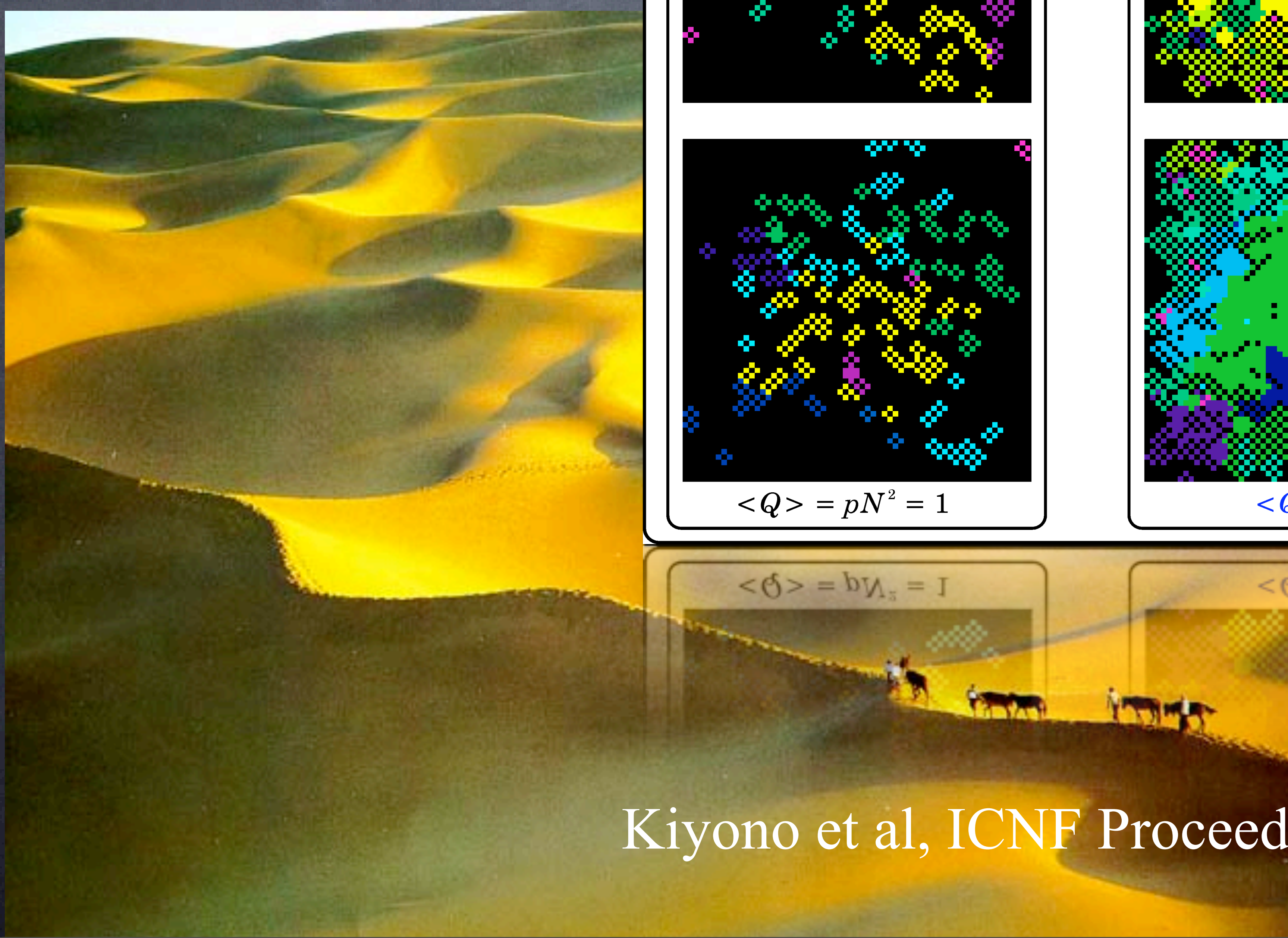
Phase transitions and critical phenomena



NOT SOC!

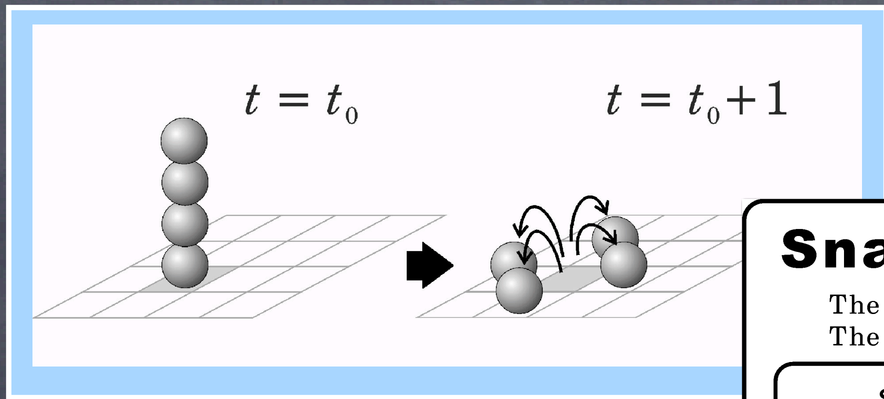
- driving rate >> 0



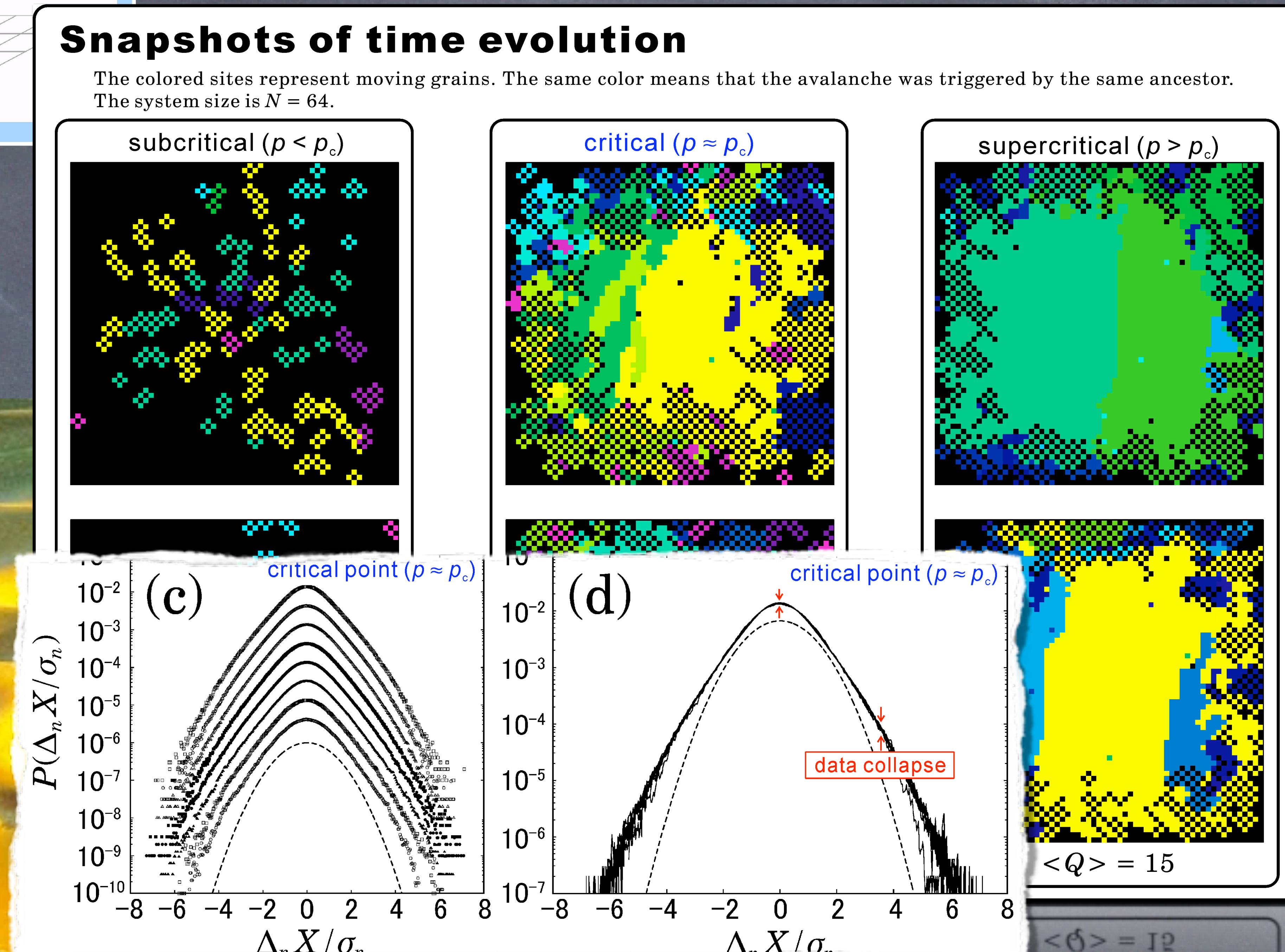


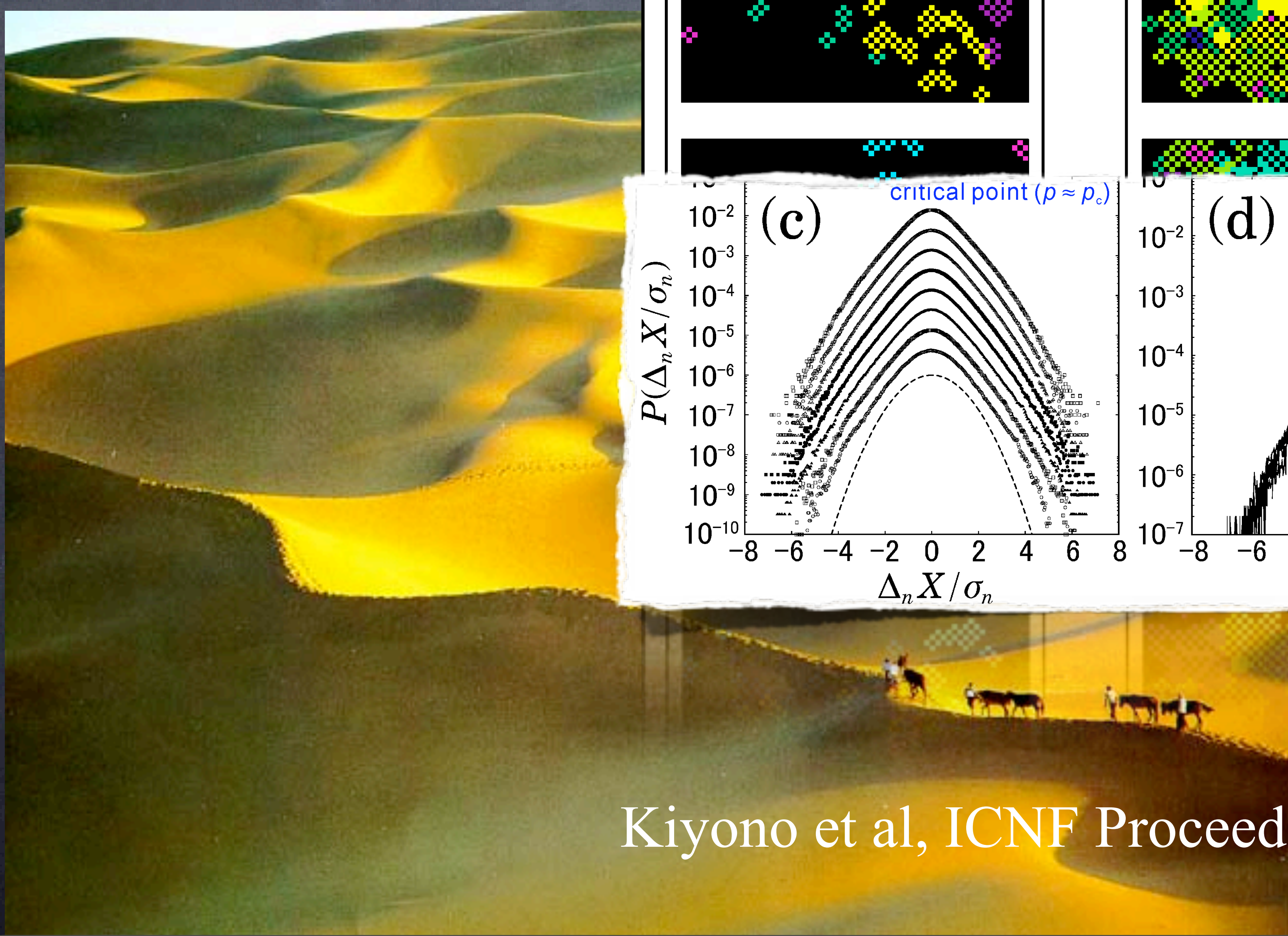
Kiyono et al, ICNF Proceedings, Salamanca, 2005

Phase transitions and critical phenomena



NOT SOC!
- driving rate >> 0

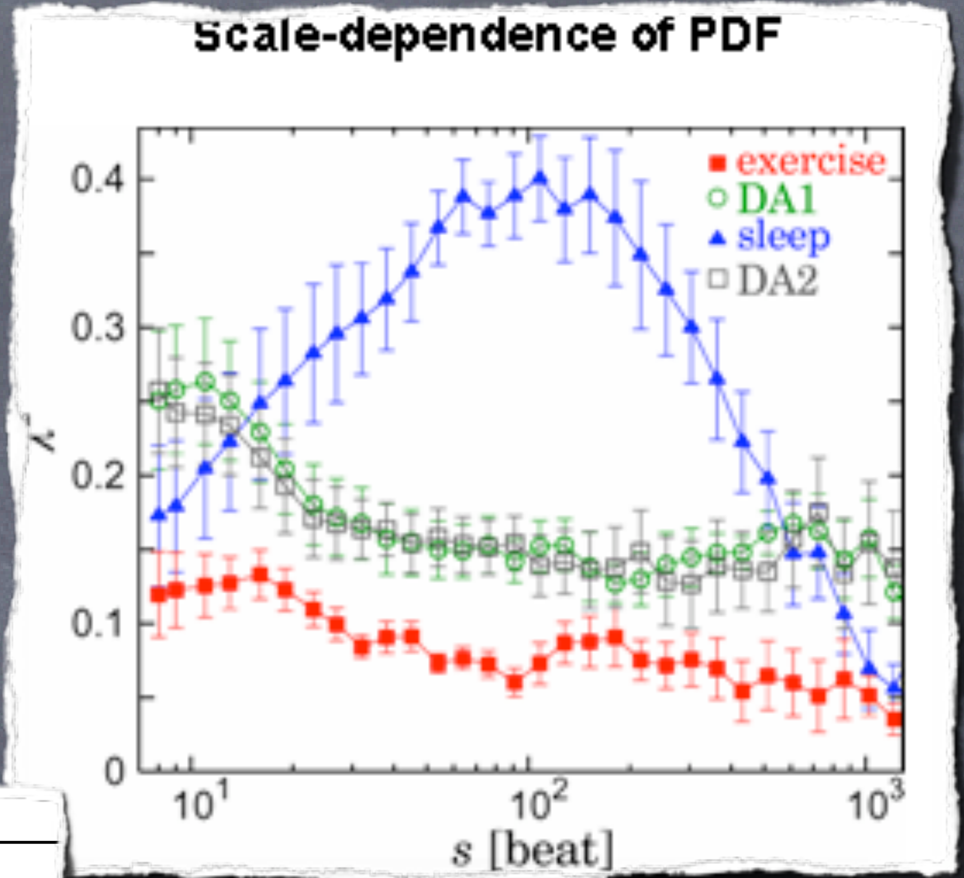


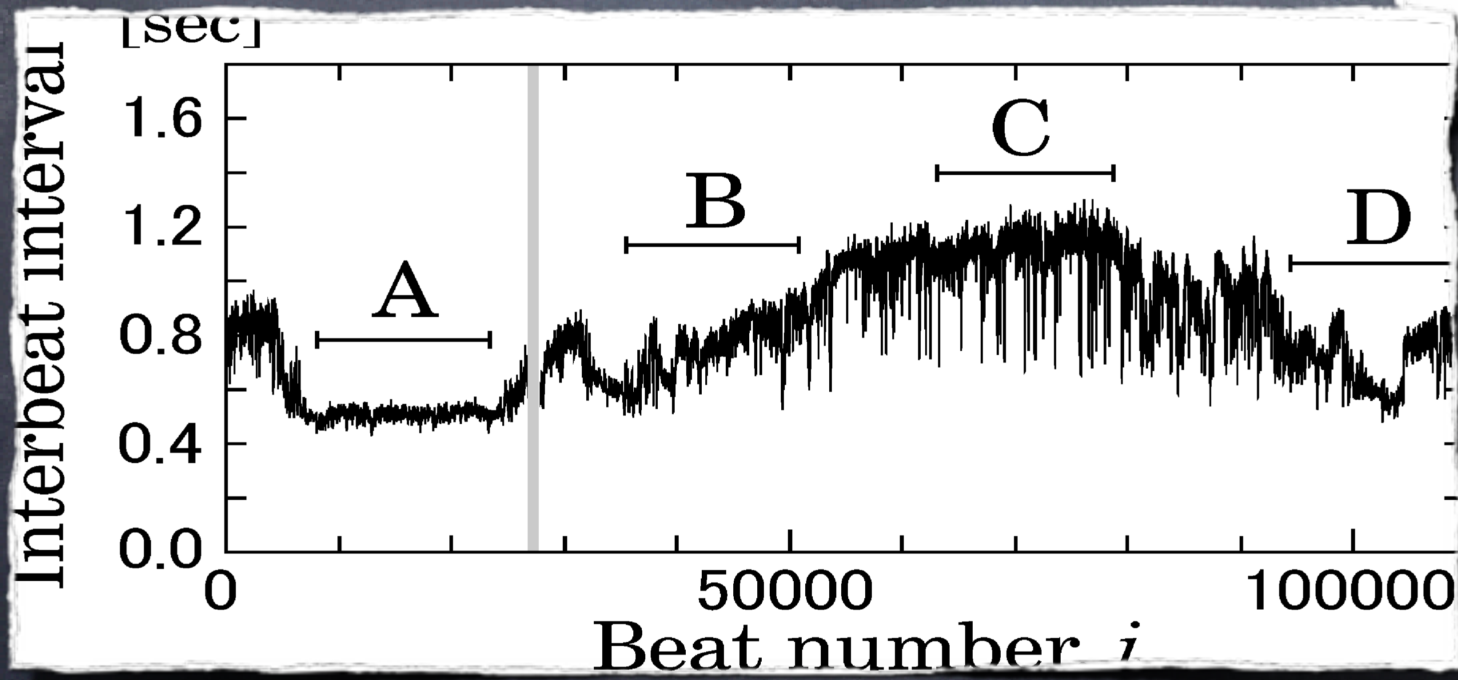


Kiyono et al, ICNF Proceedings, Salamanca, 2005

Phase transition in healthy human HRV - K. Kiyono et al, PRL 95, 2005.

- heartbeat intervals measured for 24 hours (13:00--)
- seven healthy subjects (mean age 25.3)
- three physiological states:
  - normal daily activity
  - experimental exercise
  - controlled sleep





also confirmed in a model
K. Kotani et al, PRE, 2005

Two point magnitude correlation function (Arneodo et al, PRL 1998)

Let's define local scalewise energy:

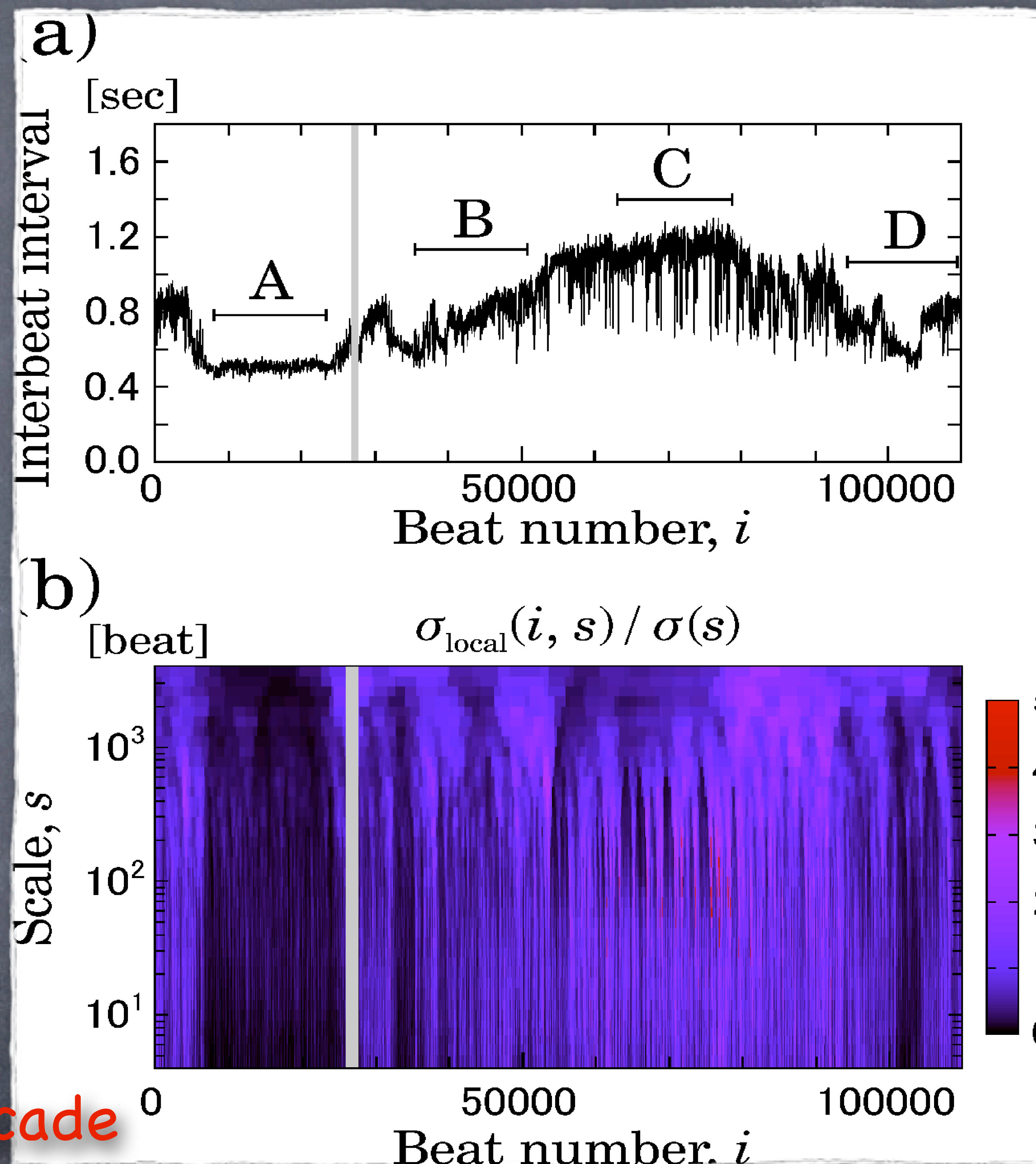
$$\sigma_s^2(i) = \frac{1}{s} \sum_{j=1+s(i-1)}^{si} \Delta_s B(j)^2$$

and its magnitude:

$$\bar{\omega}_s(i) = \frac{1}{2} \log \sigma_s^2(i)$$

The magnitude correlation function:

$$C(\tau, s_1, s_2) =$$
$$= \langle (\bar{\omega}_{s_1}(i) - \langle \bar{\omega}_{s_1} \rangle)(\bar{\omega}_{s_2}(i+\tau) - \langle \bar{\omega}_{s_2} \rangle) \rangle$$

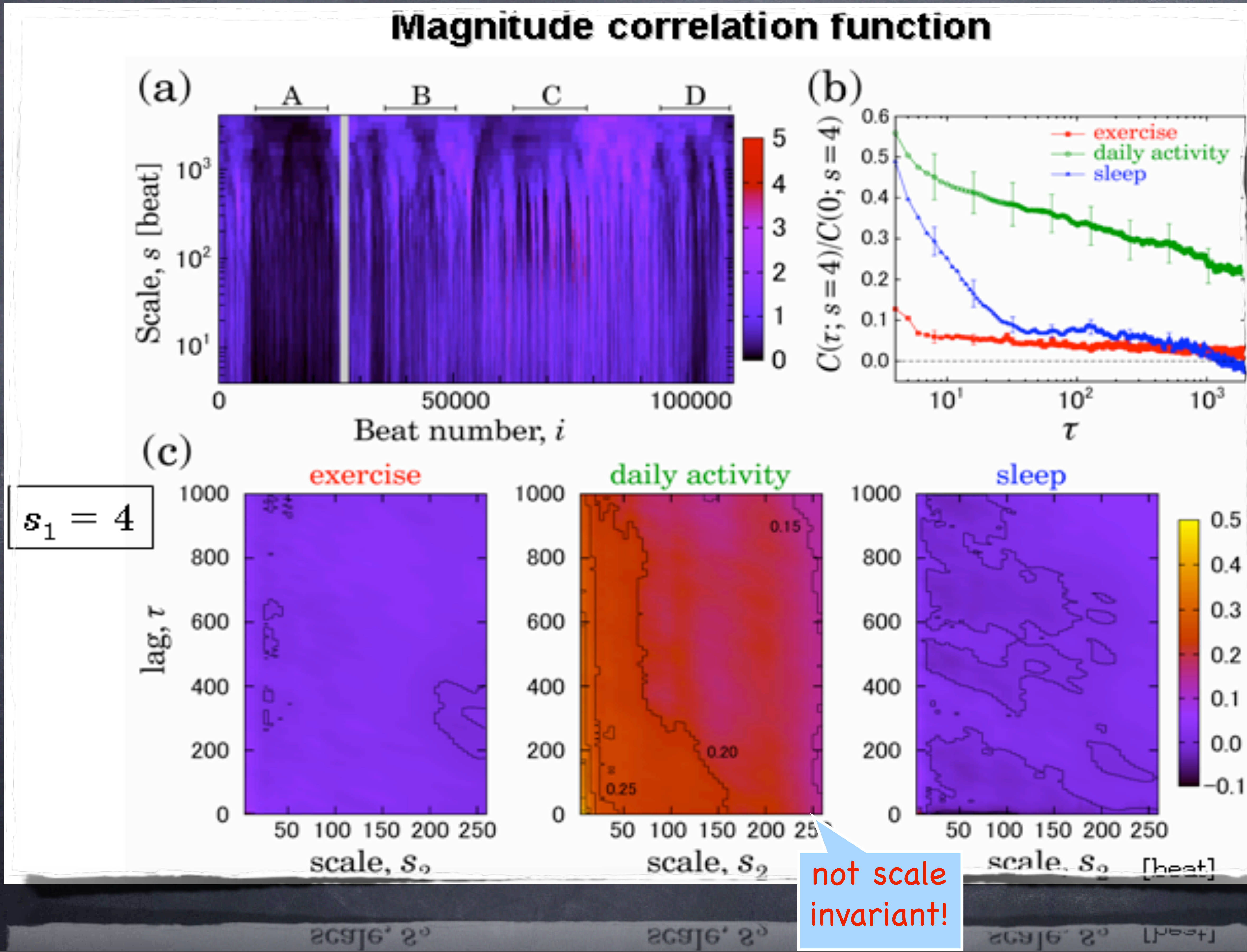


C is invariant for multiplicative cascade

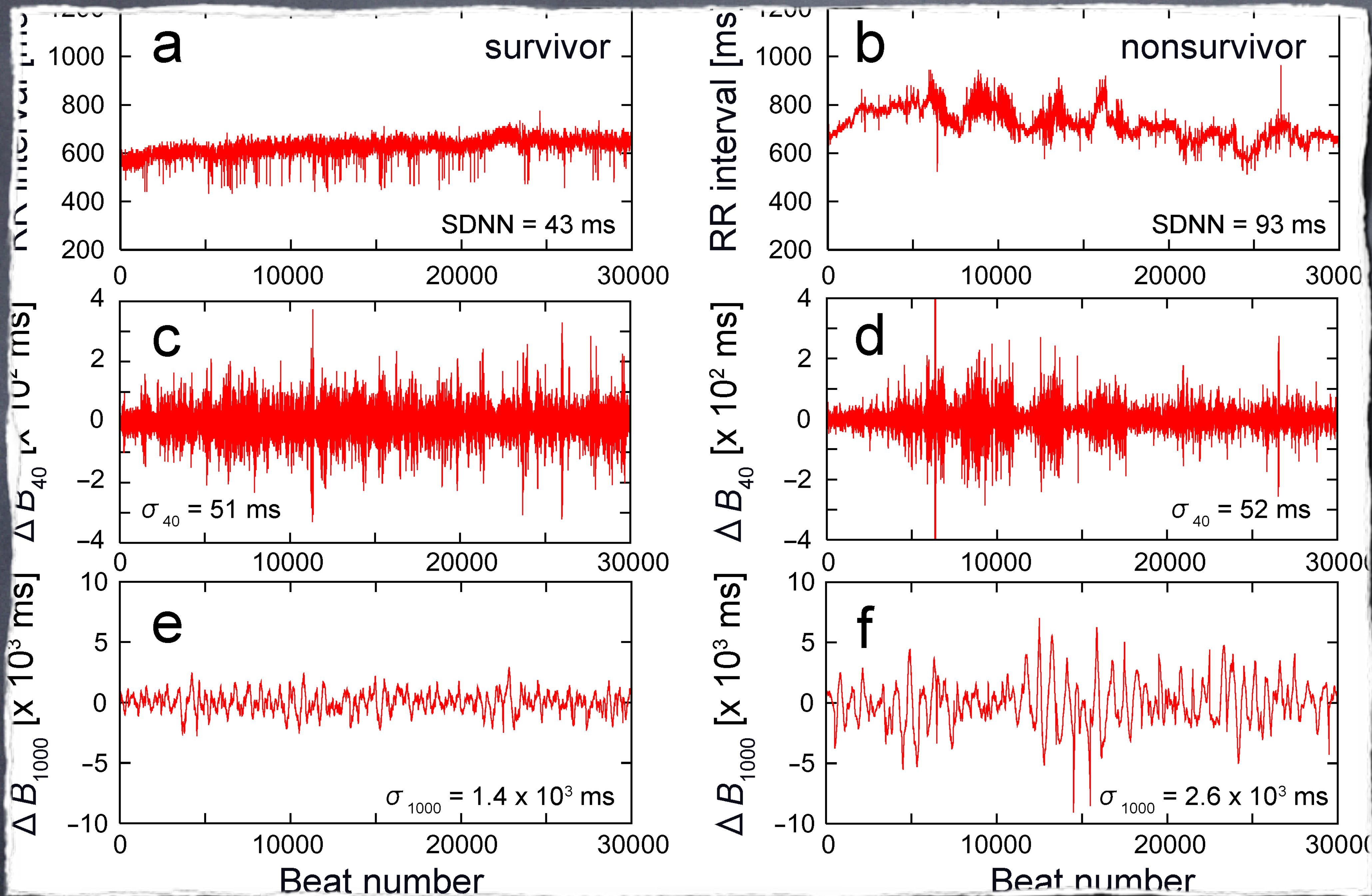
"one-scale" magnitude correlation: $s_1 = s_2$

"two-scale" magnitude correlation: $s_1 > s_2$

Phase transition scenario in healthy human HRV confirmed with two-point magnitude correlation function - K. Kiyono et al, PRL 95, 2005.

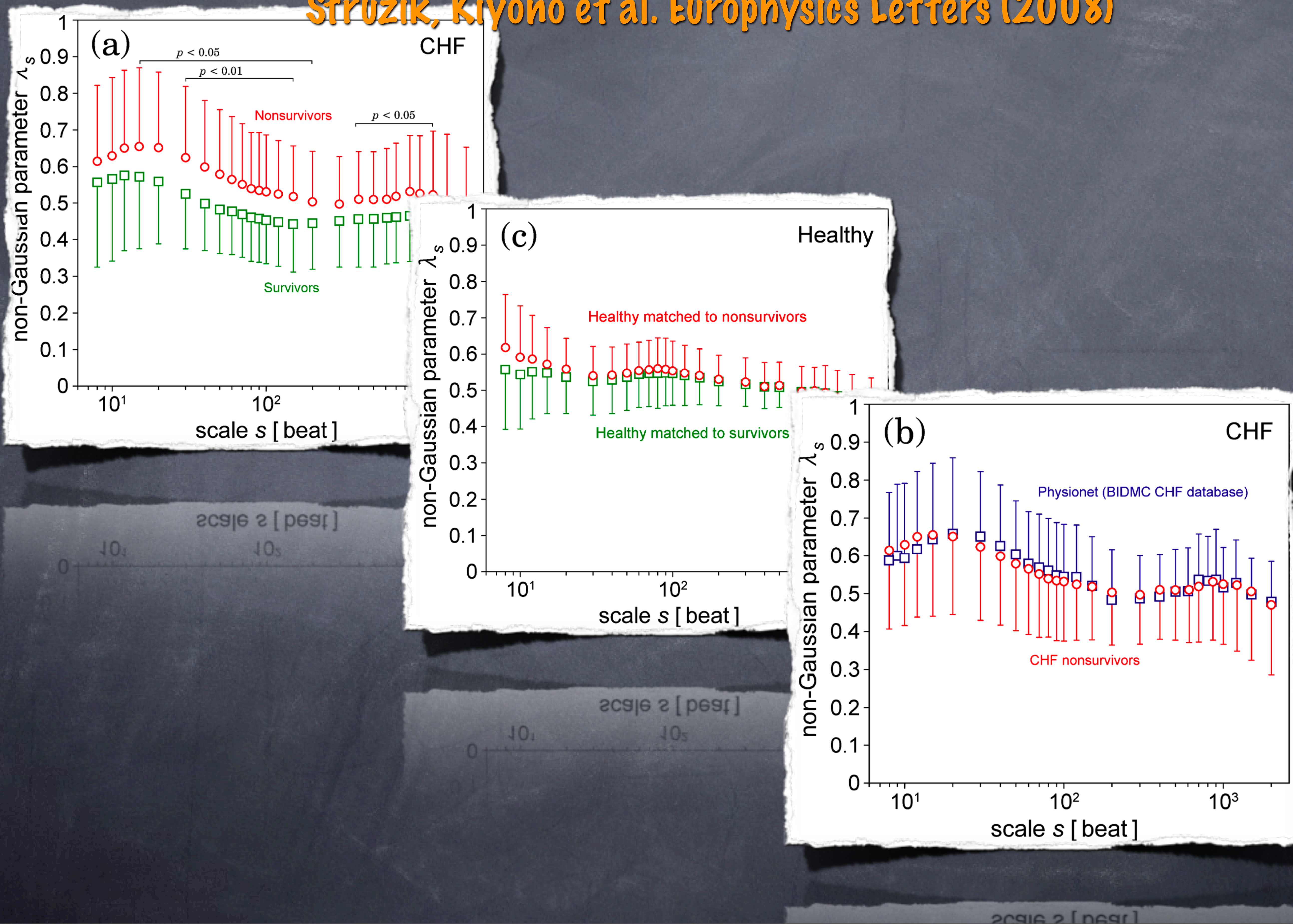


Heart rate variability of patients with congestive heart failure (CHF)

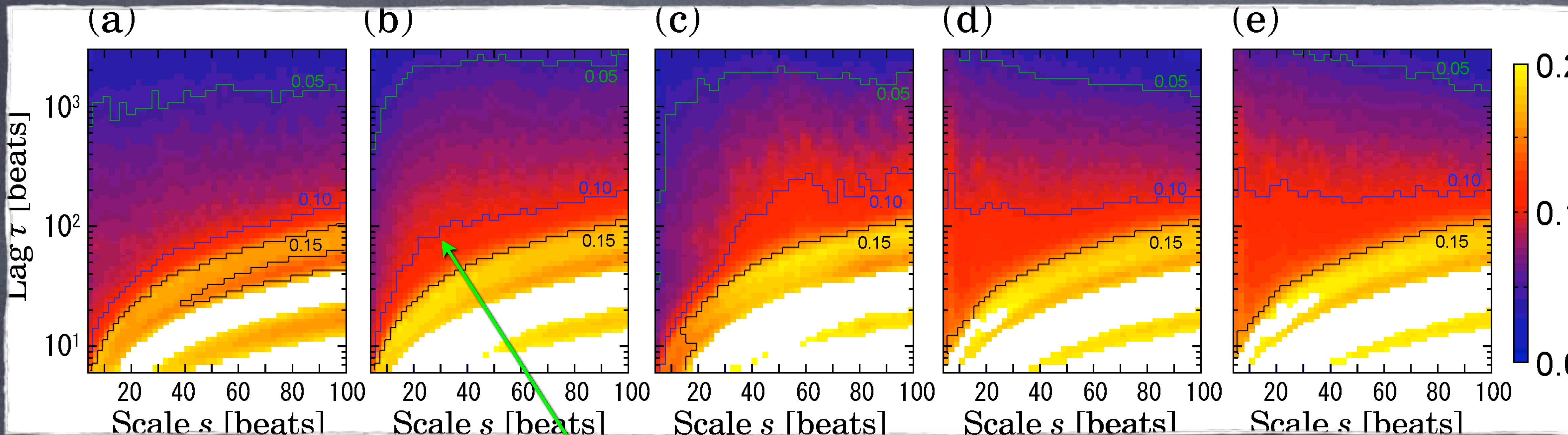


(108 CHF patients)

"Increased Intermittency of Heart Rate in Fatal Heart Failure"
Struzik, Kiyono et al. Europhysics Letters (2008)



"Increased Intermittency of Heart Rate in Fatal Heart Failure"
Struzik, Kiyono et al. Europhysics Letters (2008)



increased two-point correlations at ~40 bpm

survivors

non-survivors

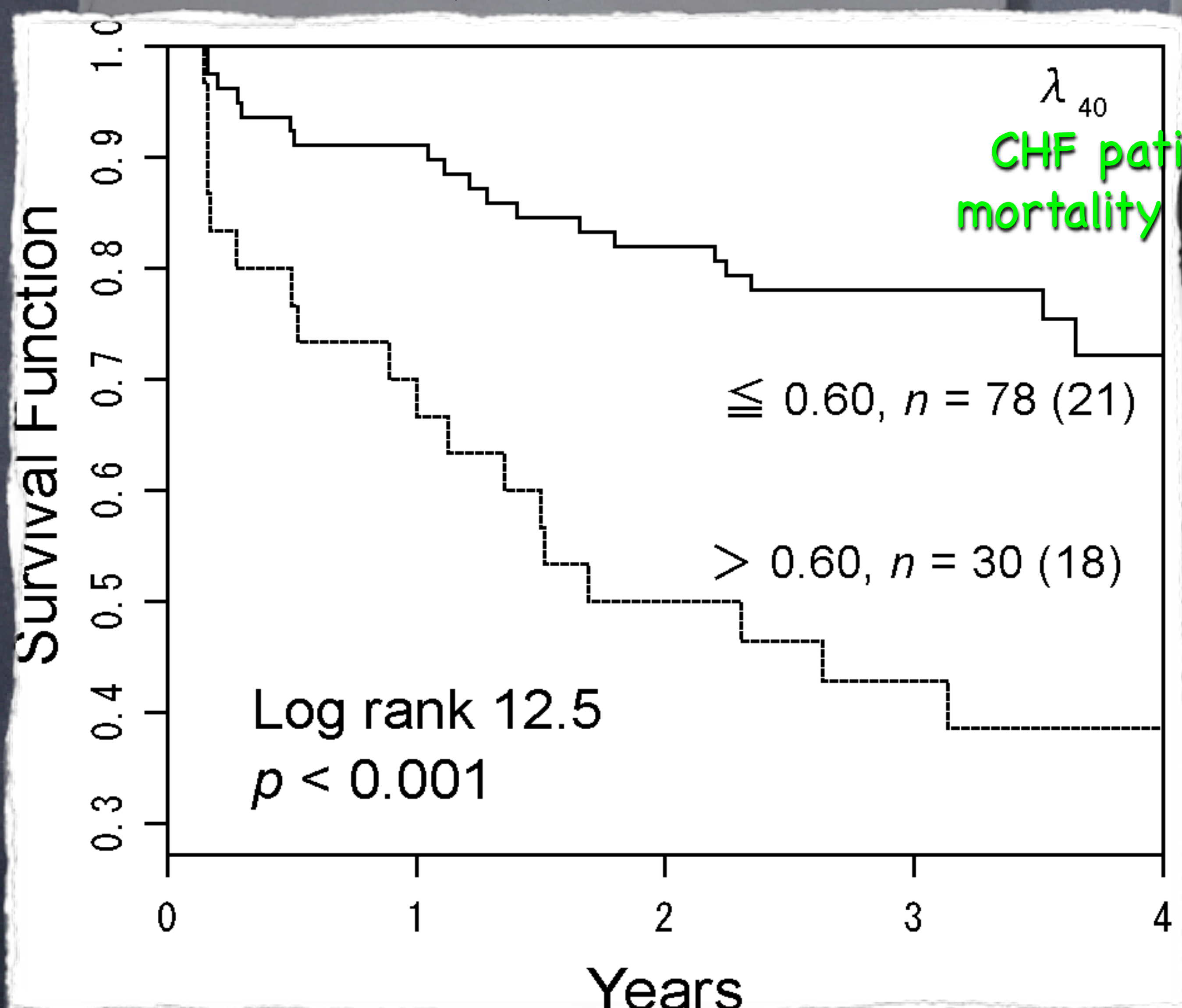
Physionet CHF

healthy matched to survivors

healthy matched to non-survivors

Non-Gaussian parameter λ as an independent risk predictor

Covariate	Hazard ratio (95% CI)	χ^2	P value	SD
Age	1.03 (1.00–1.05)	5.46	0.020	
ischaemia	1.97 (1.04–3.73)	4.55	0.036	
ln BNP	2.26 (1.45–3.53)	13.3	0.00031	1.06



	Survivor ($n = 69$)	Non-survivor ($n = 39$)	P value
Mean R-R interval, ms	771 ± 139	770 ± 116	0.985
SDNN, ms	78 ± 35	80 ± 34	0.750
SDANN, ms	68 ± 63	60 ± 59	0.525
rMSSD, ms	40 ± 43	38 ± 39	0.808
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
VLF power ms^2	1258 ± 1210	935 ± 992	
ln	6.6 ± 1.2	6.3 ± 1.2	0.293
LF power ms^2	675 ± 1576	620 ± 1055	
ln	5.4 ± 1.5	5.6 ± 1.5	0.932
HF power ms^2	988 ± 2572	975 ± 1735	
ln	5.6 ± 1.5	5.6 ± 1.5	0.992
LF/HF ratio	1.2 ± 1.1	1.1 ± 1.2	0.792
α_1 $(4-11$ beats)	0.78 ± 0.26	0.82 ± 0.22	0.429
α_2 $(11-1024$ beats)	1.03 ± 0.13	1.03 ± 0.15	0.907
λ_{10}	0.56 ± 0.23	0.63 ± 0.21	0.161
λ_{40}	0.50 ± 0.13	0.60 ± 0.18	0.0012
λ_{1000}	0.46 ± 0.13	[illegible]	0.037

CHF patients with a larger value of λ have higher mortality compared to the patients with a smaller λ.

(108 CHF patients)

"Non-Gaussian Heart Rate as an Independent Predictor of Mortality in Chronic Heart Failure Patients"

Kiyono et al. (Heart Rhythm, 2007)

Unsolved problems:

1) how to accommodate in extended cascade:

   a) critical scale invariance

   b) (increased) intermittency

2) how to accommodate the above in the S-H/K model

3) Why is Complexity of Heart Rate Increased in Congestive Heart Failure

With many thanks
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Eiichi Watanabe
Yoshiharu Yamamoto

the end

oh, there they are!