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Multi-Scale Entropy: A Framework to Quantify Health Status of Human and Machine

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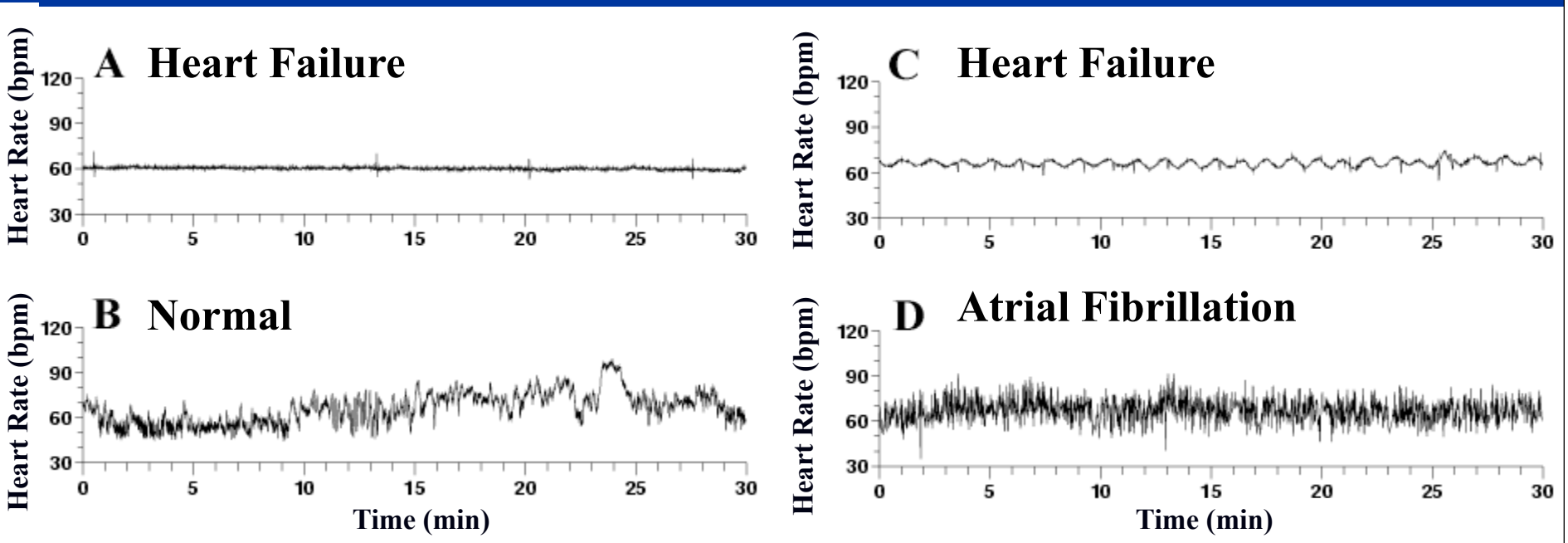
National Central University

Heart Rate Time Series

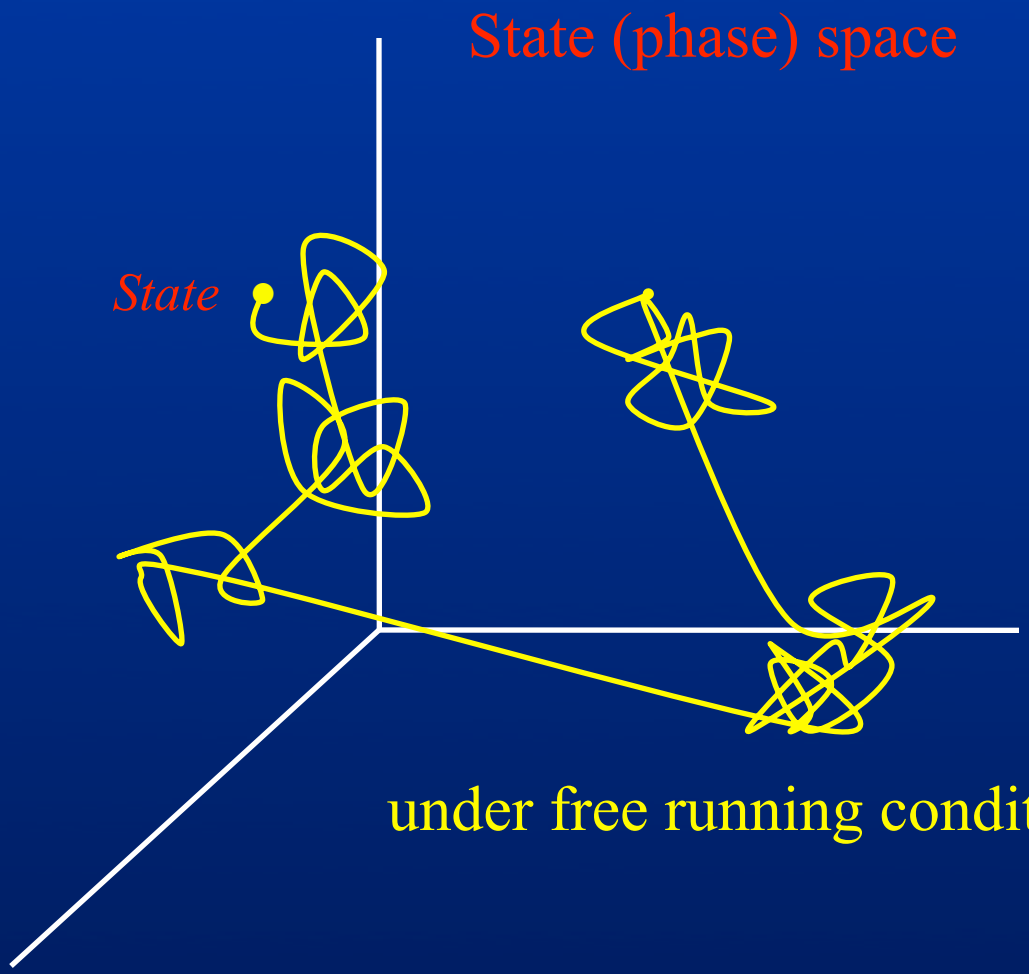


- Loss of variability is bad
- Not all variabilities are good

What is the origin of biologic/physiologic variabilities?

These variabilities (dynamical complexity) provide living systems the necessary flexibility to adapt to possible challenges

A physicist's naive view of a biological system



Health = Complexity of the dynamics

The complexity of a biological system should be a measure of the system's *capacity* to adapt and function in an ever changing environment.

Physiologic complexity should be defined by how the state space is explored in a non-random manner

Aging and disease will degrade a system's complexity

How to Measure *Complexity*?

Ideally, we want to measure the volume of state space being visited under all possible challenges.

However, two difficulties:

- It is not wise to stress the system with all conceivable challenges
- It is not feasible to record all variables of the system in order to define the state space

Possible solutions are ...

Fluctuation Dissipation Theorem

Multiple time scales

order

good variability
中庸之道

disorder

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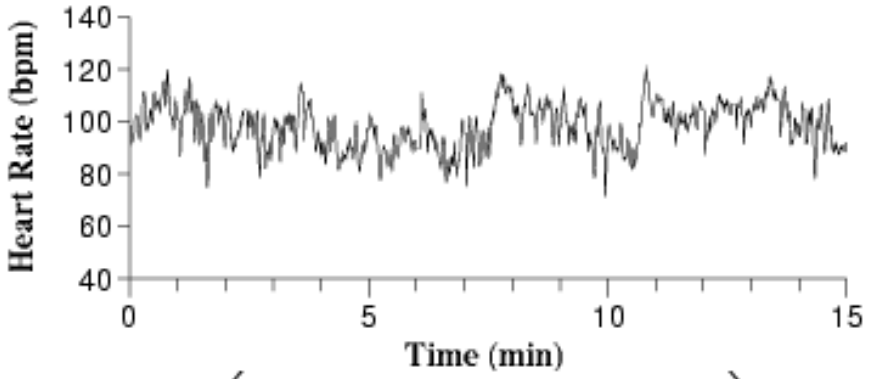
,.s rif fj/z.,eihniq fheycogo49
kvue1357 fjyir-8.g'[\axhw -

That time of year thou mayst in me behold
When yellow leaves, or none, or few, do hang
Upon those boughs which shake against the cold,
Bare ruin'd choirs, where late the sweet birds sang.

all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes jack a dull boy all work and no play makes

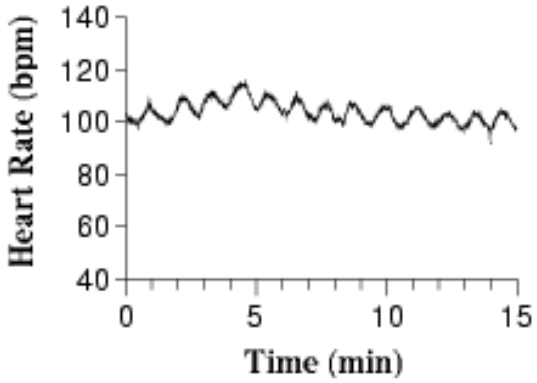
Complexity Degrades with Disease

Healthy Dynamics: Multiscale Fractal Variability

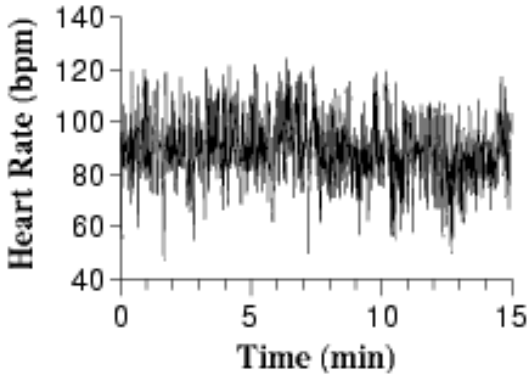


Two Patterns of Pathologic Breakdown

Single Scale Periodicity



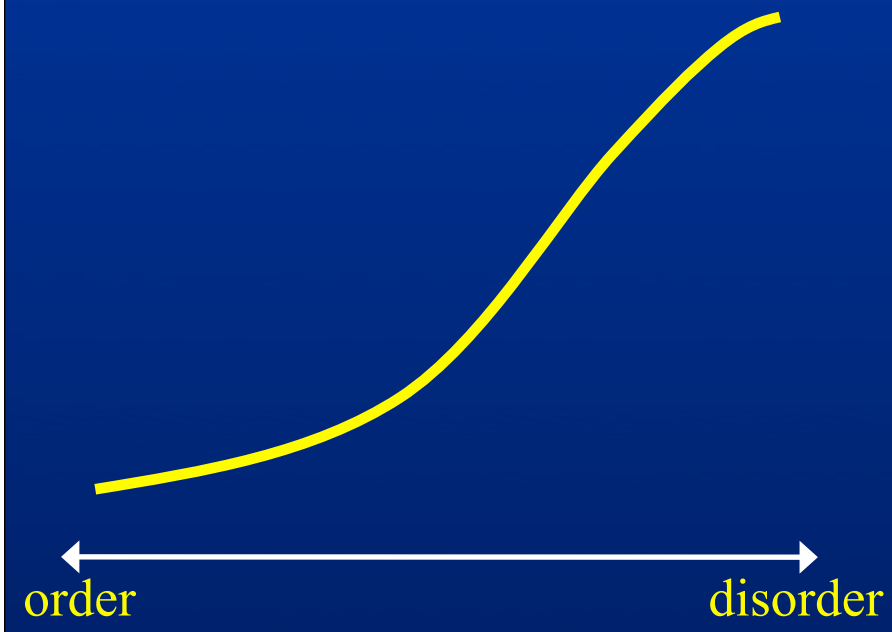
Uncorrelated Randomness



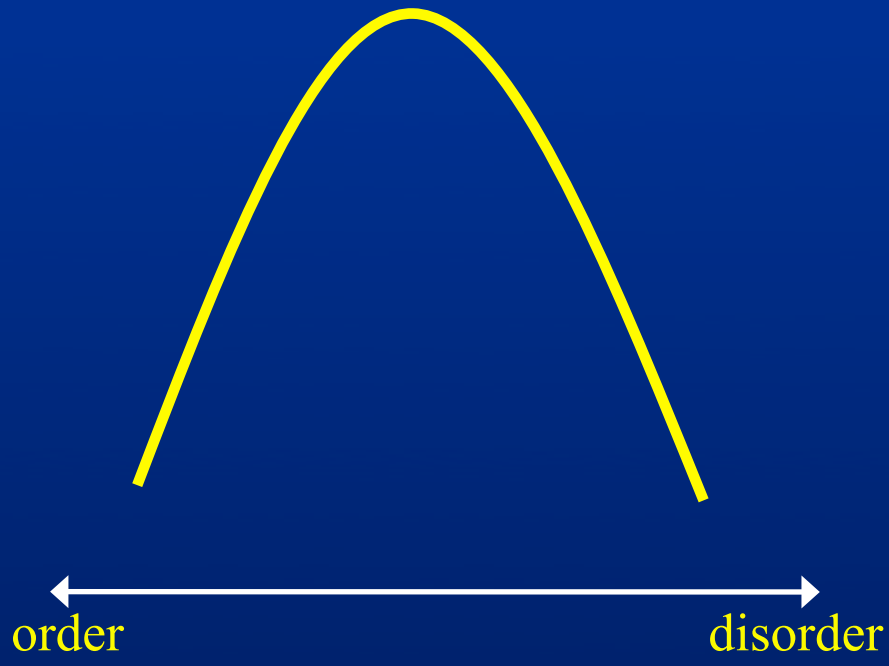
Healthy dynamics poised between too much order and total randomness.

Can entropy be used as a complexity measure?

Conventional entropy measure



Desired complexity measure



Multiscale entropy (MSE) is a quantitative measure to estimate the complexity of a system through examining the information richness of its output signal on multiple scales.

Costa, Goldberger, Peng:

Phys Rev Lett 2002;89:068102 *Phys Rev Lett* 2003;91:119802
Phys Rev Lett 2004;92:089804 *Phys Rev E* 2005; 71:021906
Europhys Lett 2007;77:68008 *Adv Adap Data Anal* 2009; 1:61

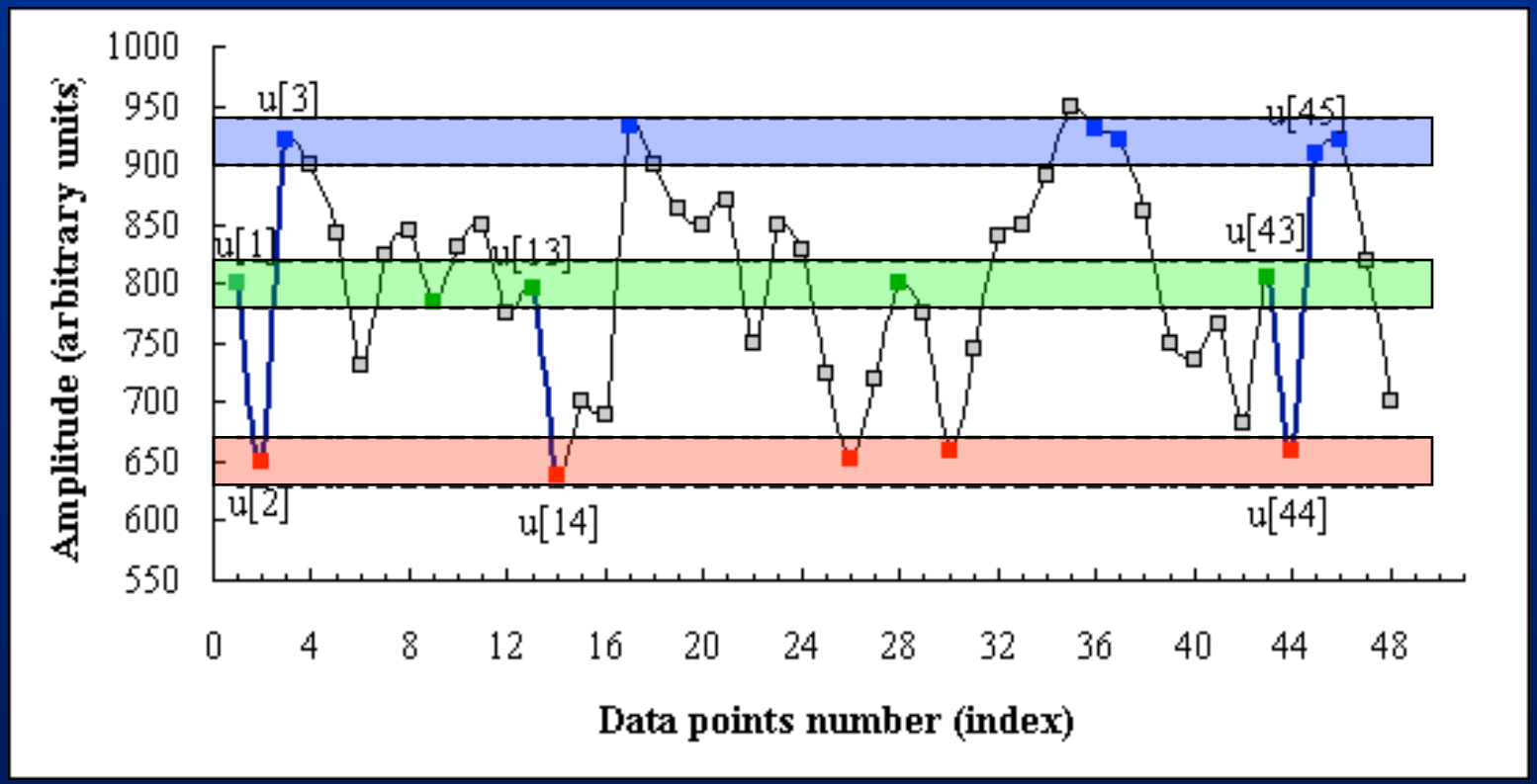
Chialvo: *Nature* 2002;419:263

Calculating Sample Entropy

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

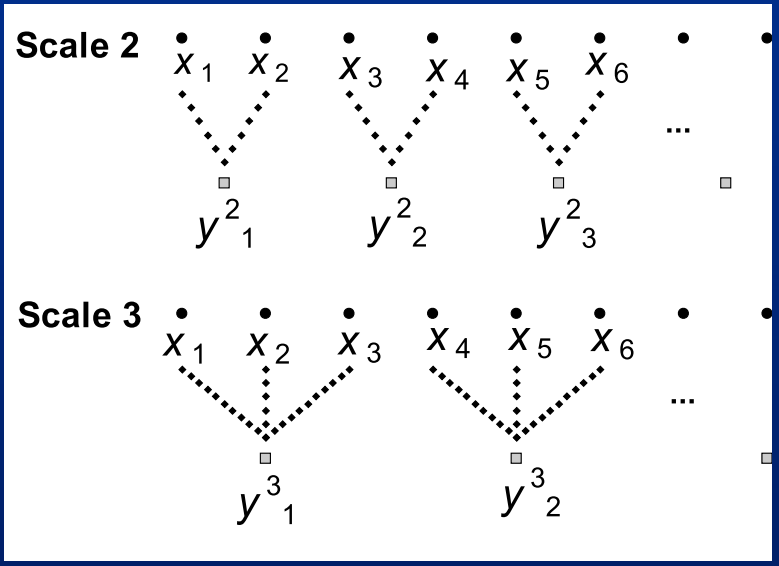
Pattern

↓

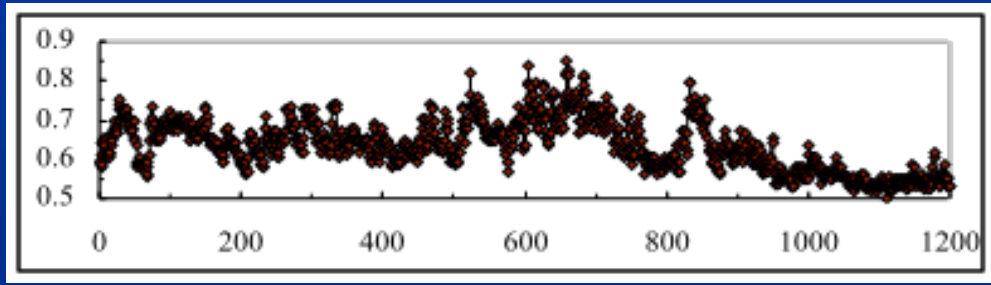


Coarse-graining procedure

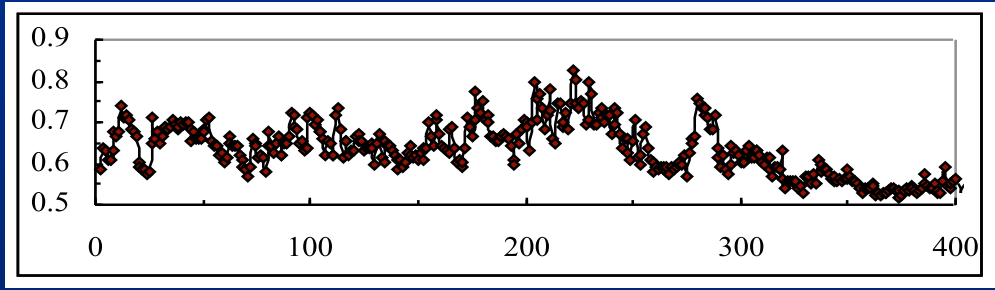
Coarse-graining schematic



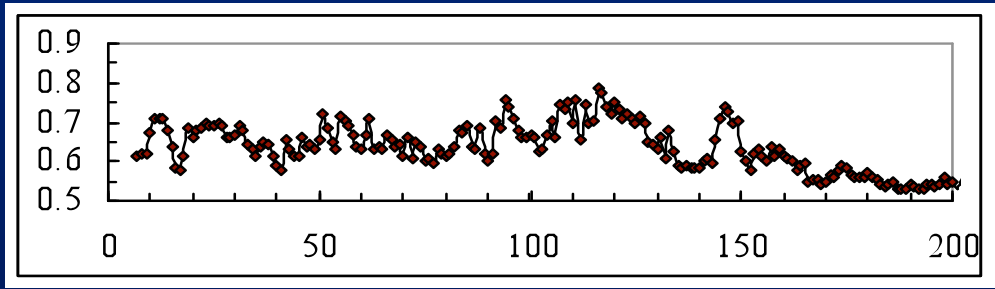
Original time series



Scale 3

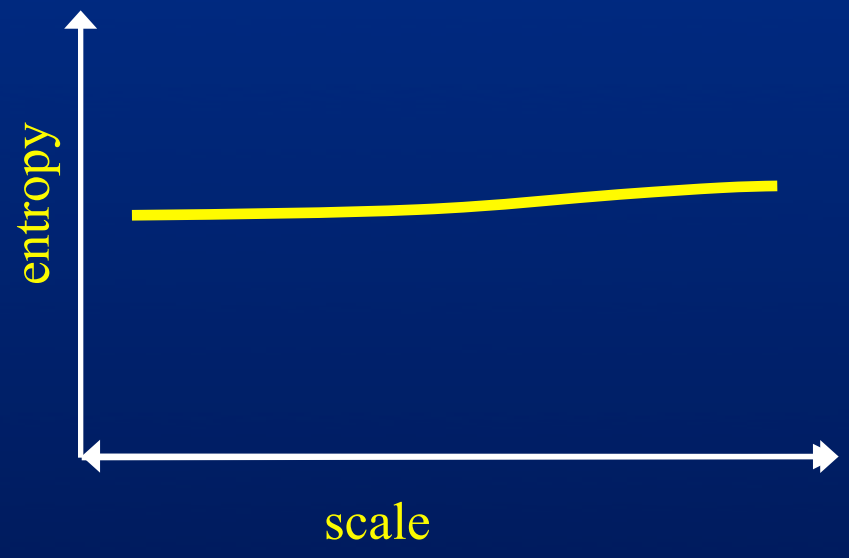


Scale 6

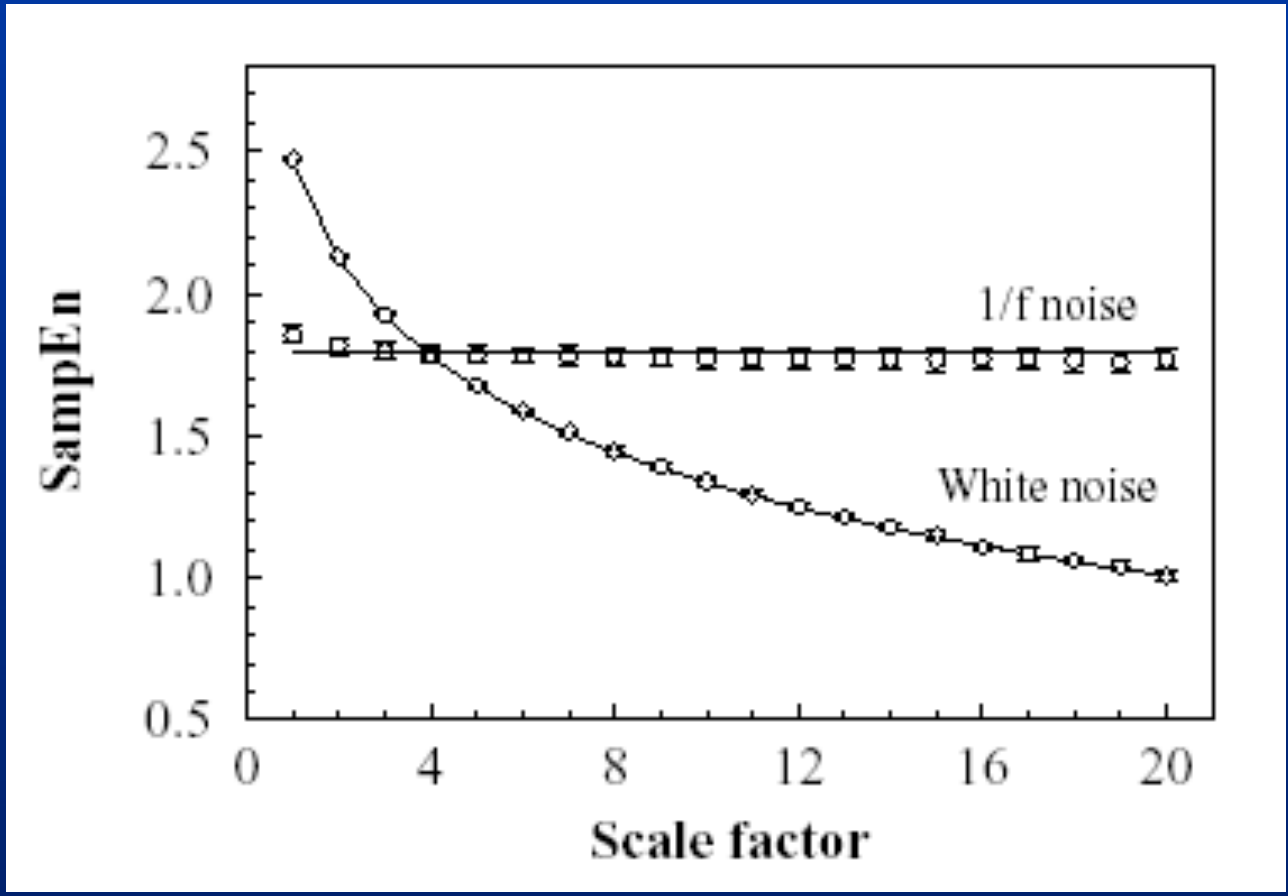


MSE algorithm

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



MSE - White and 1/*f* noises

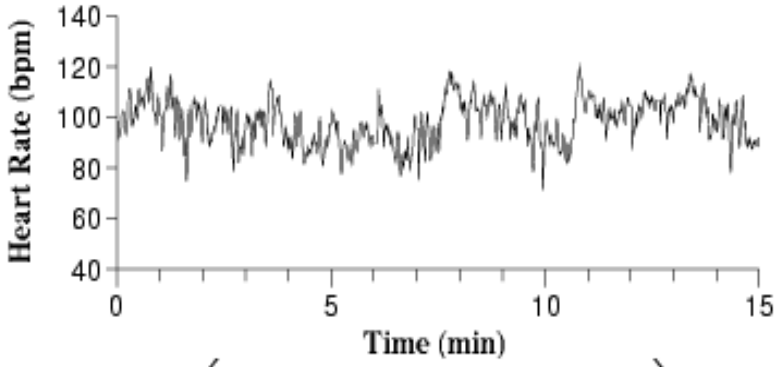


1/*f* noise is more complex than white noise

Costa *et al.* Physical Review E **71** 021906 (2005)

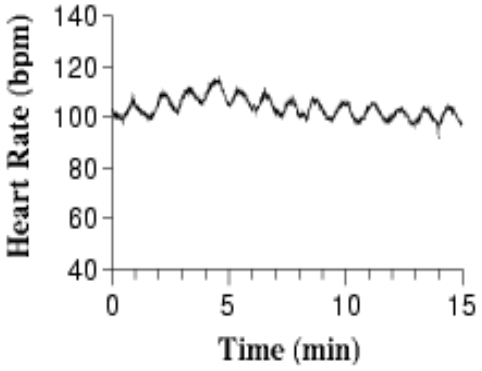
Which is the Most Complex?

Healthy Dynamics: Multiscale Fractal Variability

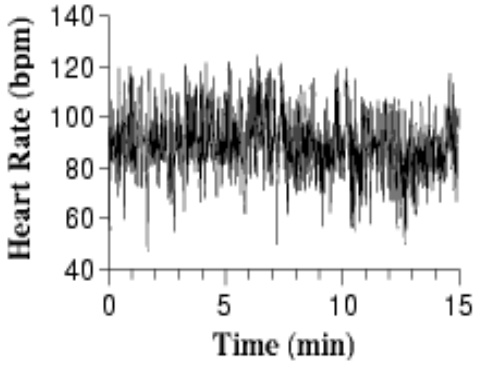


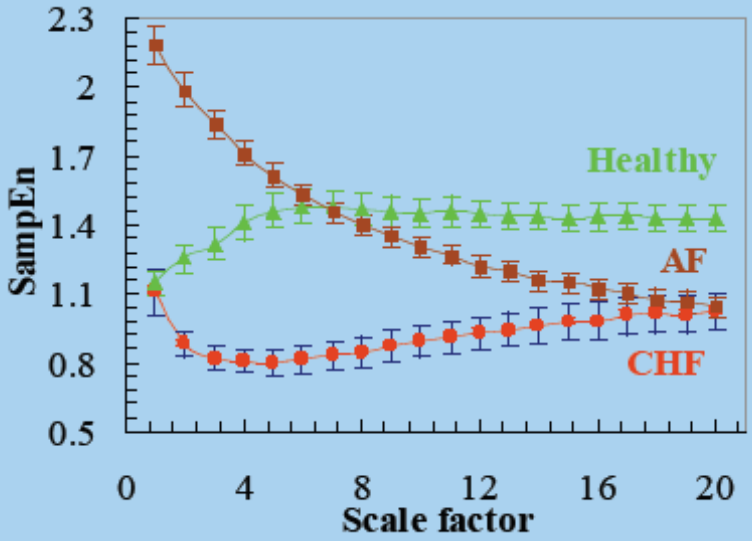
Two Patterns of Pathologic Breakdown

Order



Disorder

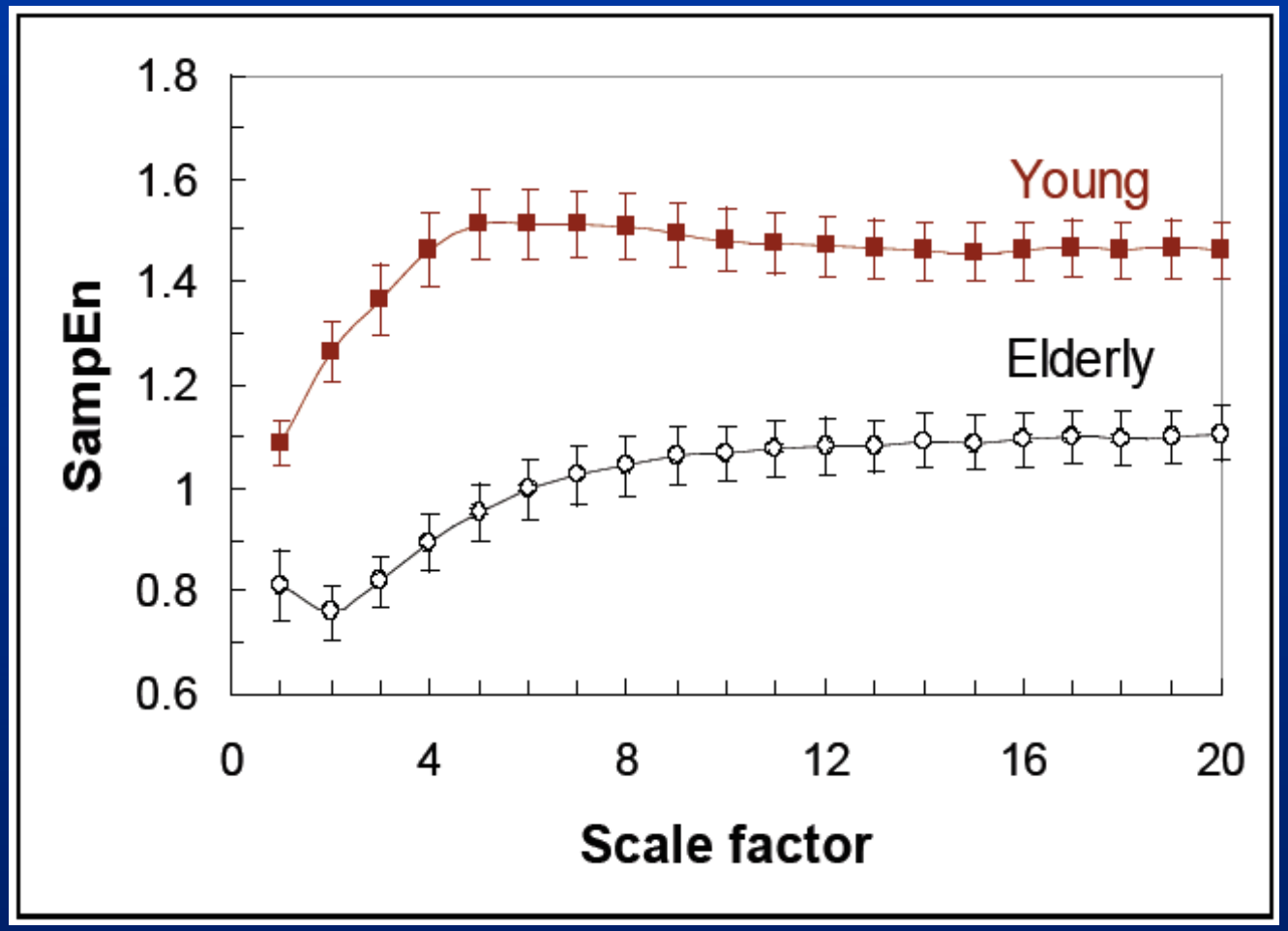




a) Healthy (n=18)
b) Chronic Heart Failure (n=15)
c) Atrial Fibrillation (n=9)

** Phys Rev Lett 2002;89:068102*

MSE Analysis for Healthy Young vs. Elderly



Young
n=20; age 32 ±6

Elderly
n=20; age 69±3

Costa *et al.* Physical Review E **71** 021906 (2005)

The Cardiac Arrhythmia Suppression Trial (CAST)

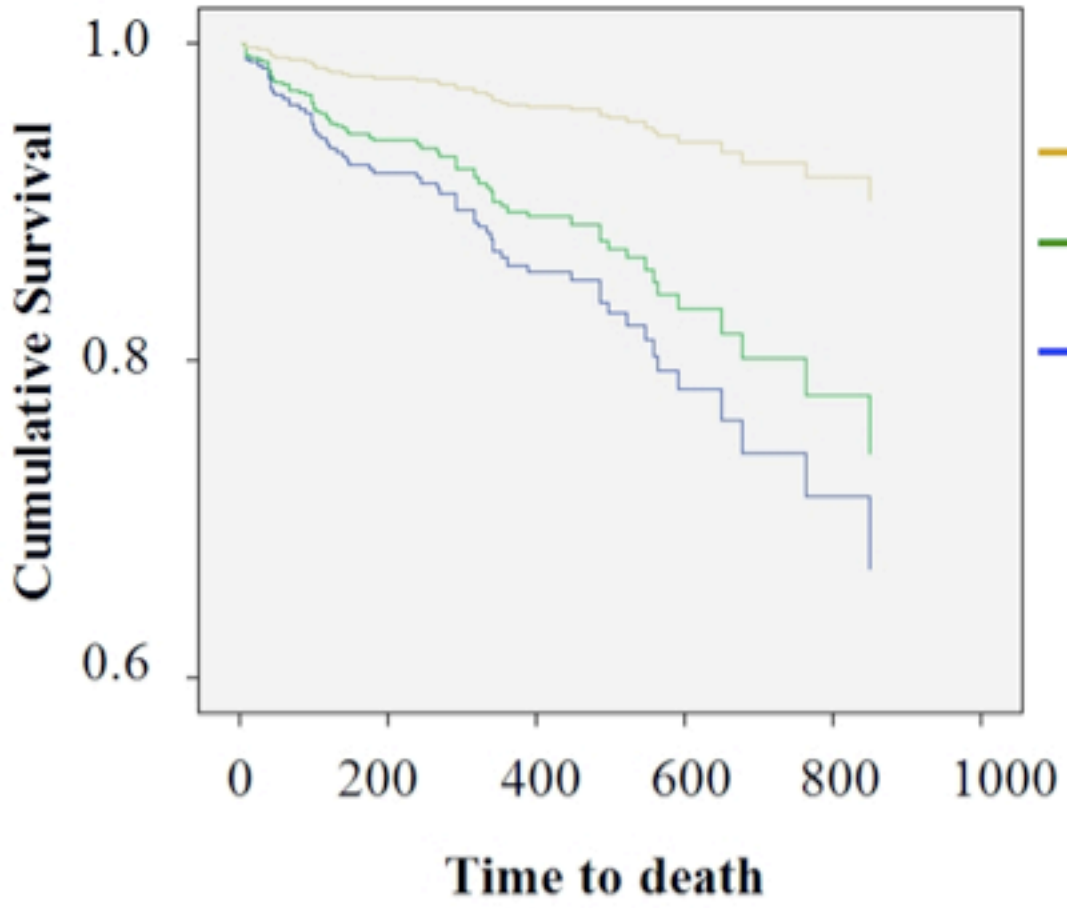
- CAST: famous study designed to test the hypothesis that the suppression of isolated premature ventricular complexes (PVCs) in survivors of myocardial infarction (heart attack) would decrease the number of deaths from sustained ventricular arrhythmias
- Patients were randomly assigned to receive encainide, flecainide, moricizine (anti-arrhythmic drugs) or placebo

The drugs are effective in removing PVC

However, The survival rate was significantly higher for patients taking the placebo than for the groups taking the anti-arrhythmic drugs (i.e., drugs could be “killers”)

The study was discontinued!

Complexity and Biotoxicity: CAST



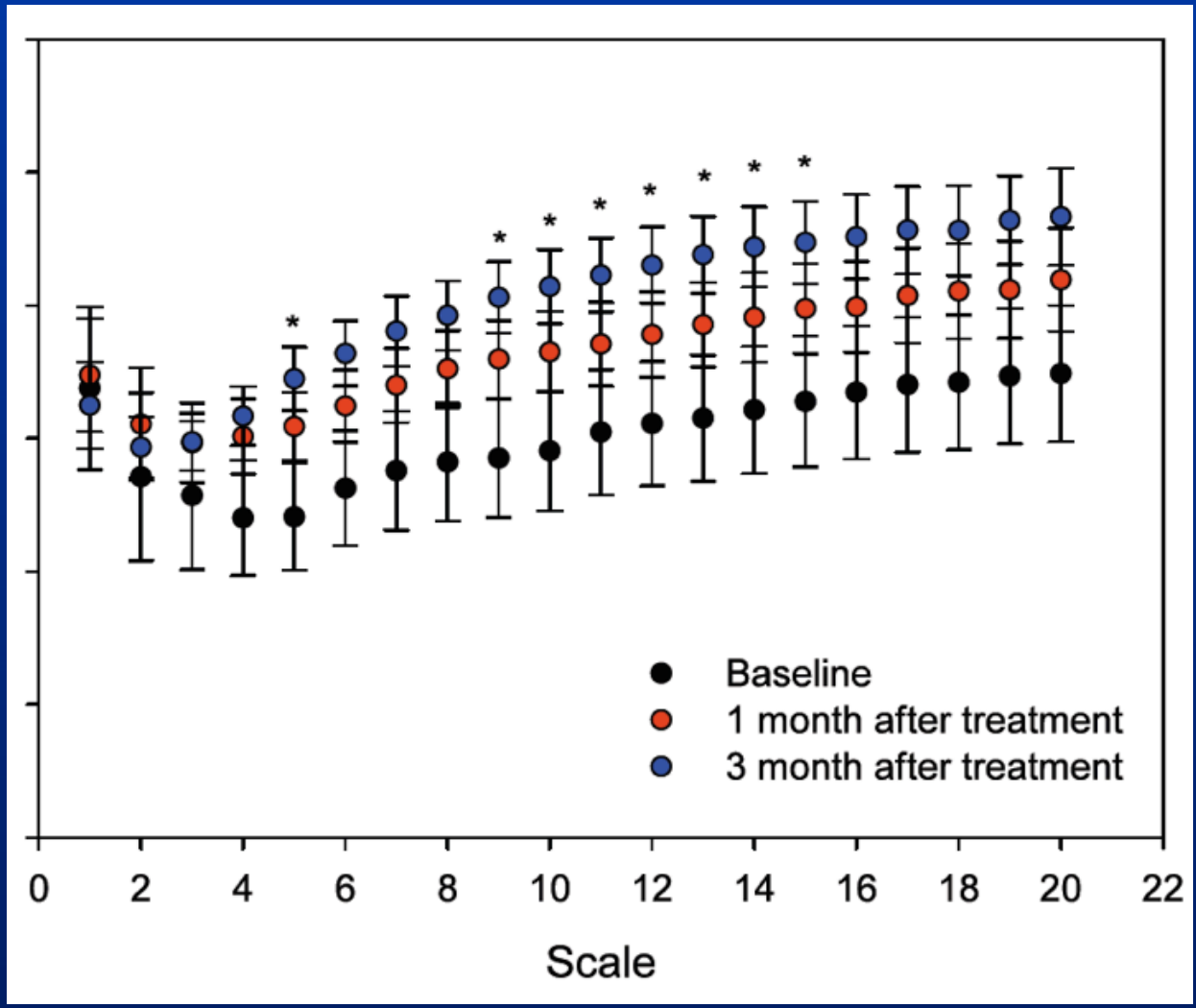
Complexity ↑ (N=225)

Complexity ↔ (N=216)

Complexity ↓ (N=292)

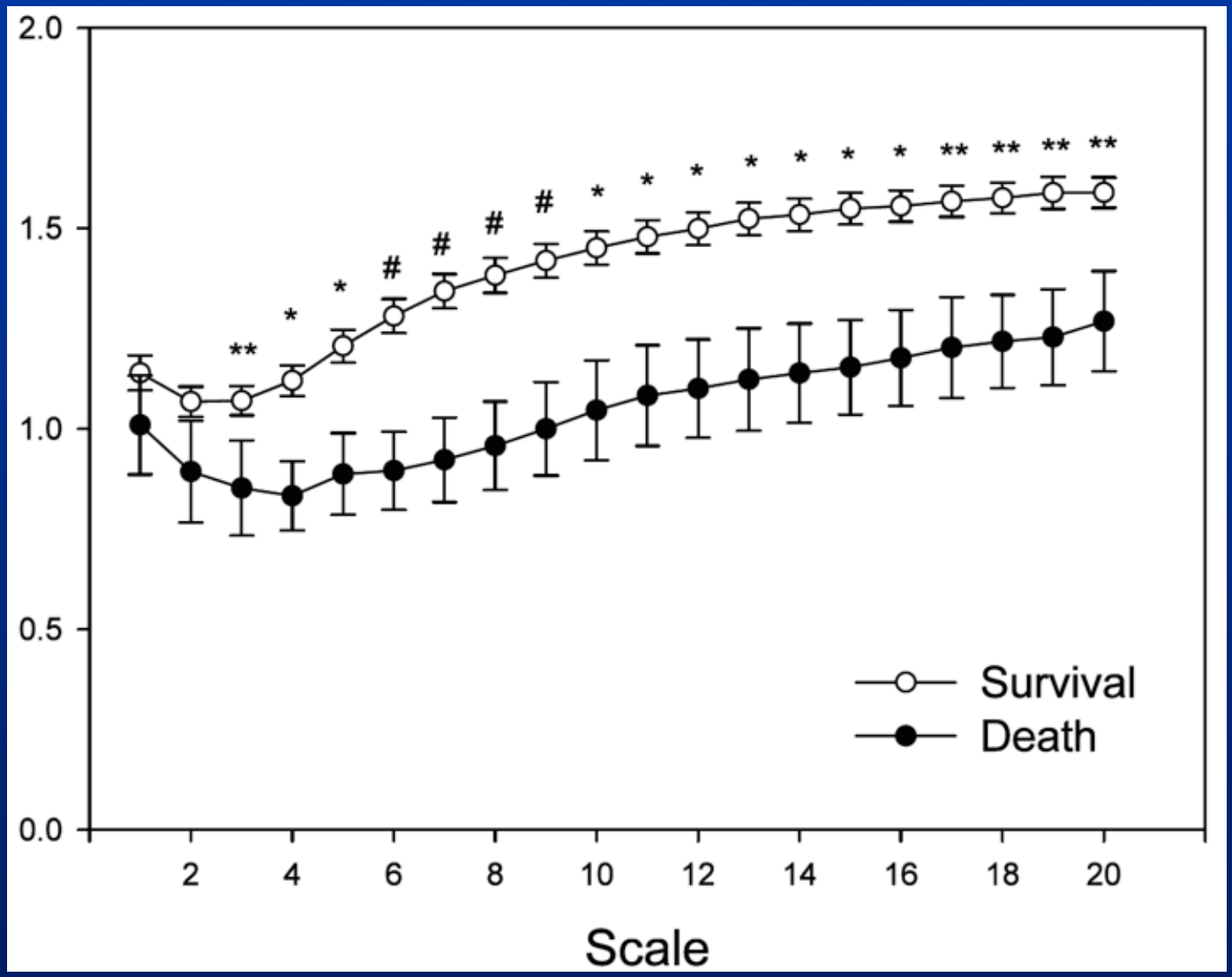
$p < 0.001$ (lower curves versus upper curve)

Beta blockers



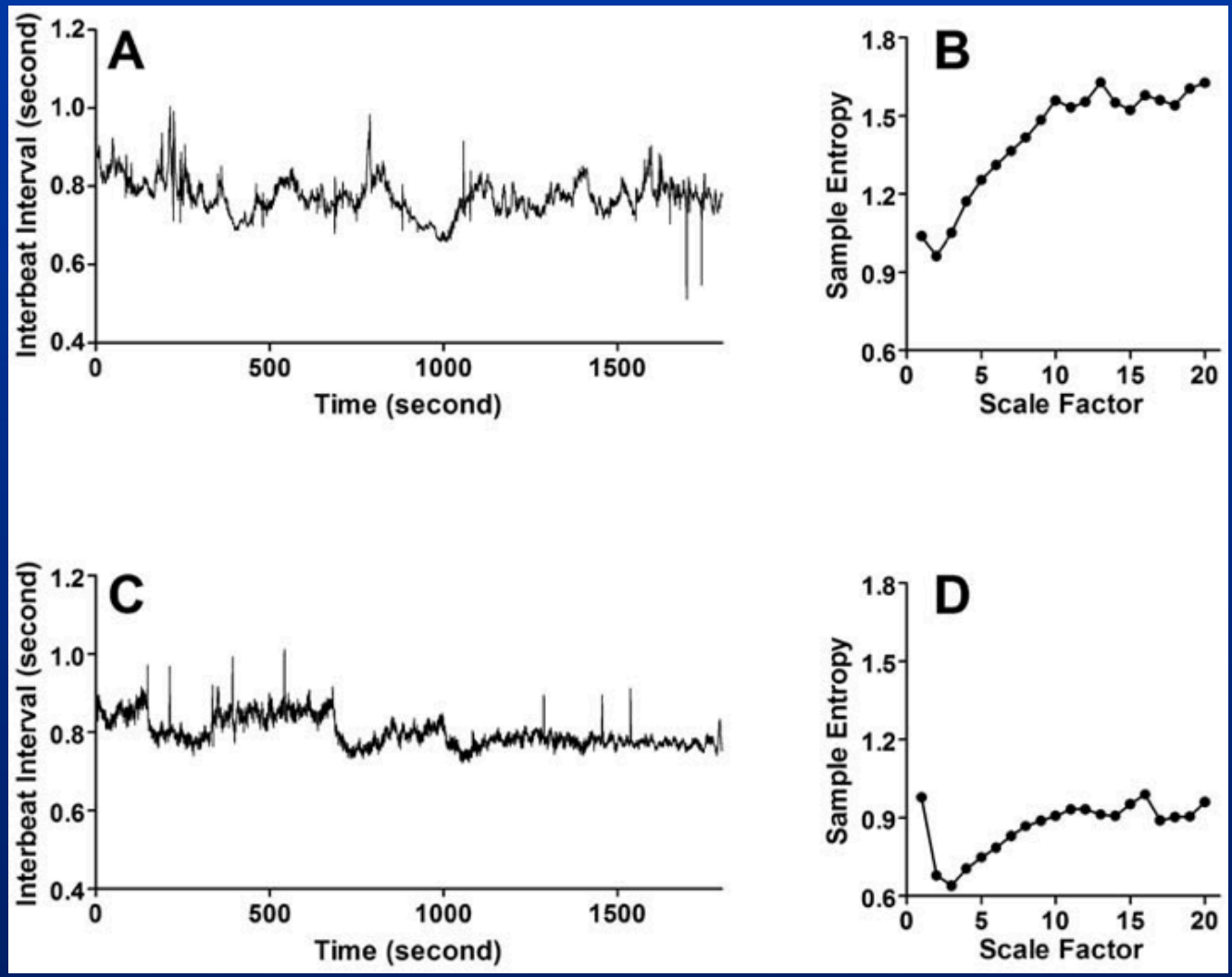
Lin *et al.* National Taiwan University Hospital

Prognosis value of complexity biomarker



Ho *et al.* National Taiwan University Hospital

From Genomes to Complexity



Chen, Tsai, Hong, and Yang. PLoS ONE 2009; **3**:e7733.

Other applications of complexity

- Center of pressure (COP) complexity:
  - Evaluate the risk of fall in elderly
  - Effectiveness of interventions for peripheral neuropathy patients
- EEG complexity and seizure
- Red blood cell membrane vibration complexity
- Machine health monitoring

Center of Pressure (COP) Experiments

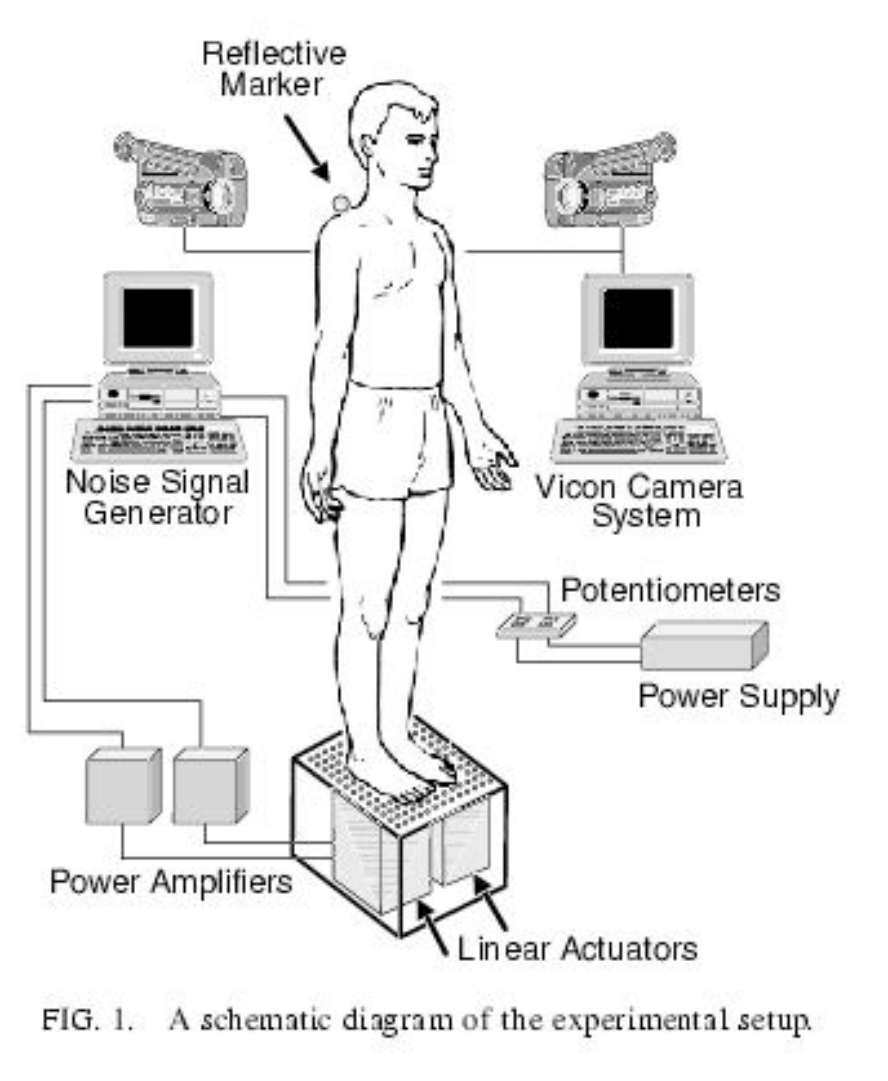


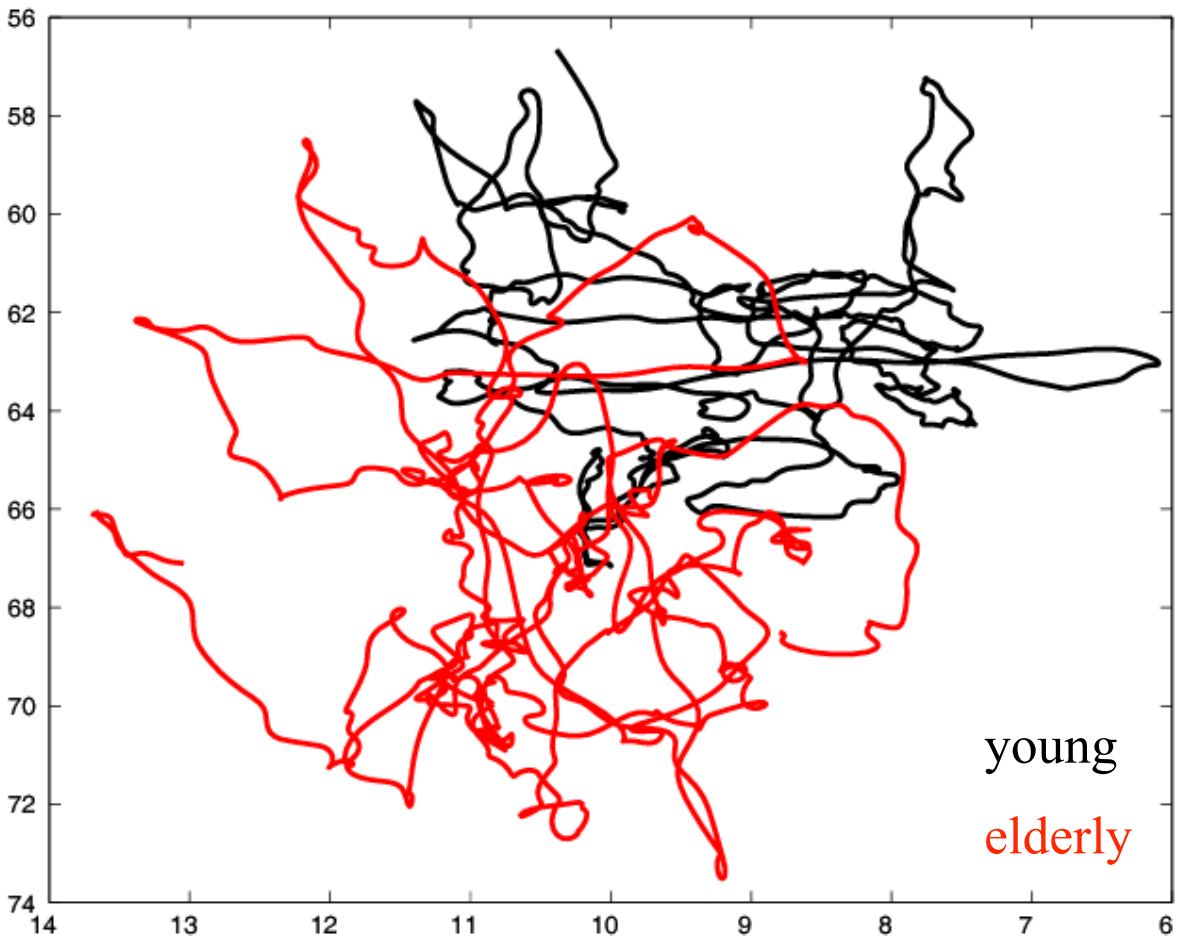
FIG. 1. A schematic diagram of the experimental setup.

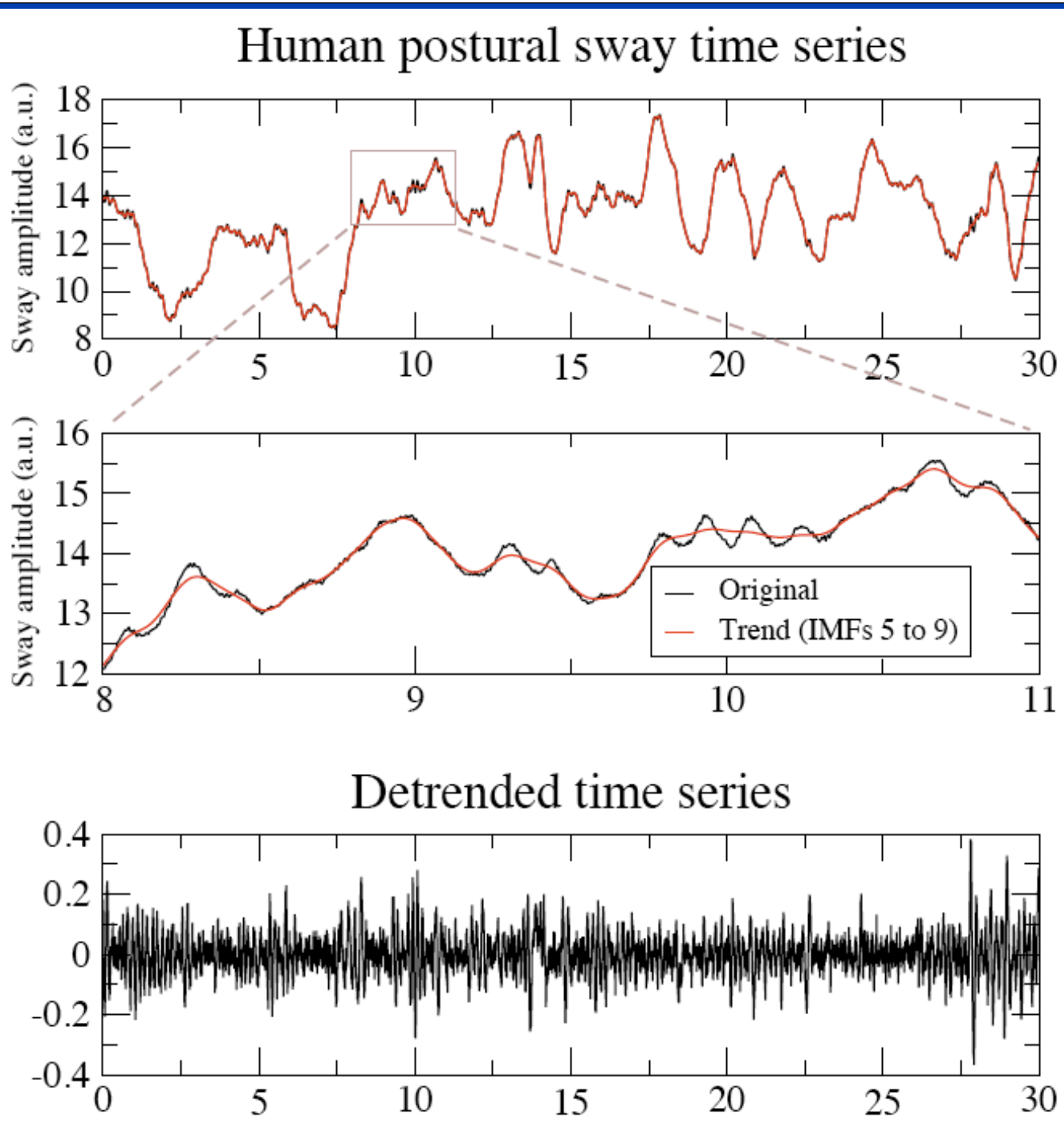
- **Experiment I – Analysis of COP (sway) dynamics**
  - 15 healthy young
  - 22 healthy elderly
  - 22 fallers
- **Experiment II – Noise-Enhanced Human Balance Control *#**
  - 15 healthy young
  - 12 healthy elderly

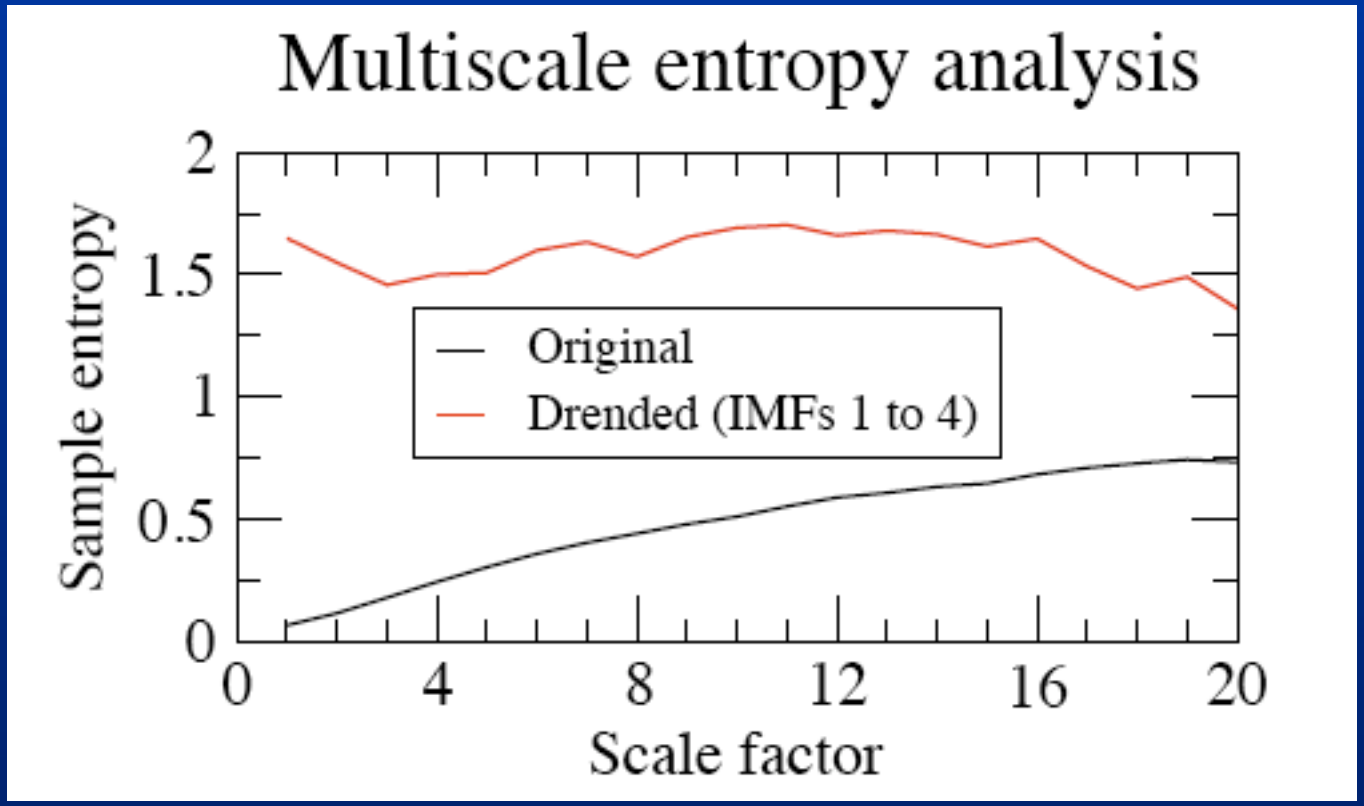
*A Priplata, J Niemi, J Harry, LA Lipsitz, and JJ Collins. Lancet 2003;**362**:1123.

A Priplata, J Niemi, M Salen, J Harry, LA Lipsitz, and JJ Collins. PRL 2002;**89**:238101

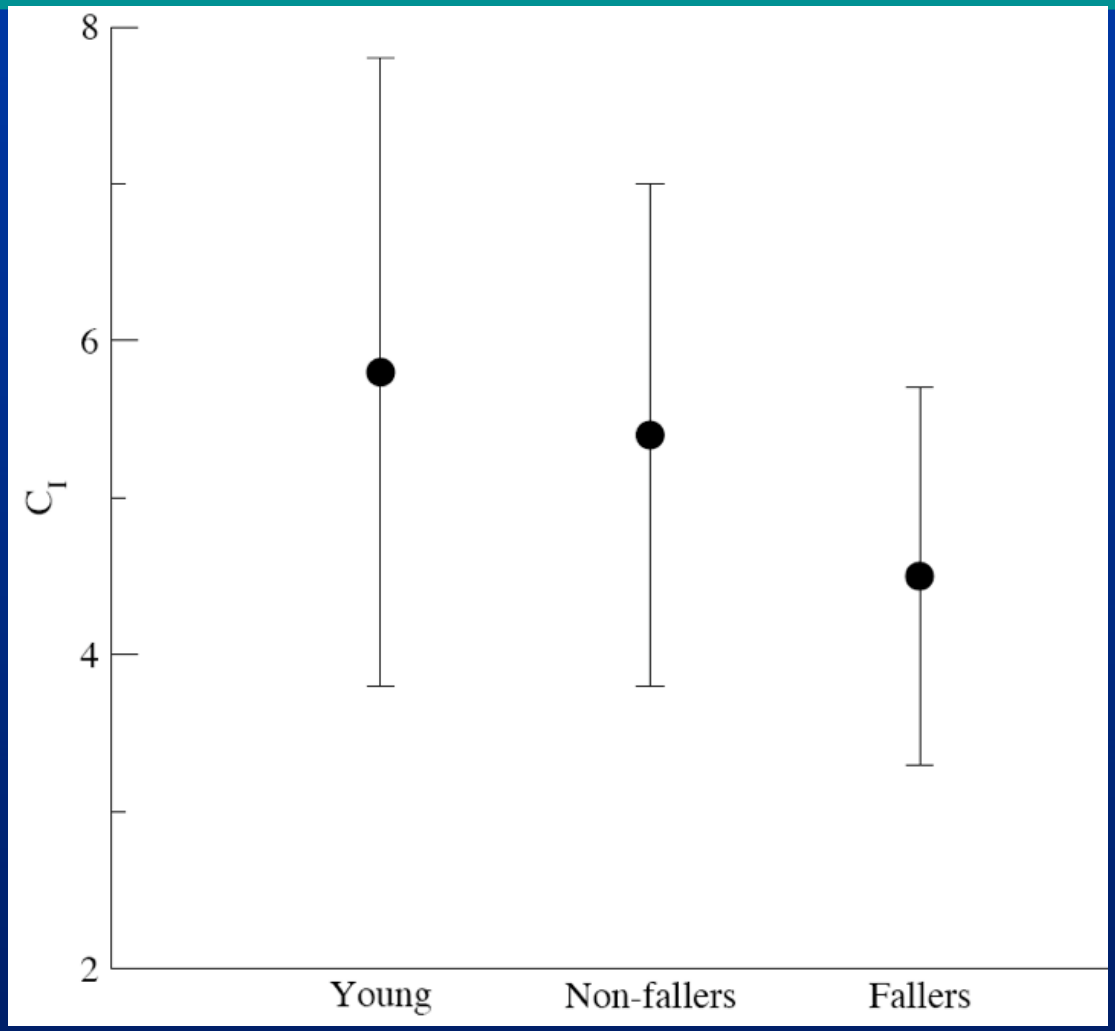
Example: center of pressure data




Human postural sway time series
Sway amplitude (a.u.)
18
16
14
12
10
8
0
5
10
15
20
25
30
Sway amplitude (a.u.)
16
15
14
13
12
8
9
10
11
Original
Trend (IMFs 5 to 9)
Detrended time series
0.4
0.2
0
-0.2
-0.4
0
5
10
15
20
25
30

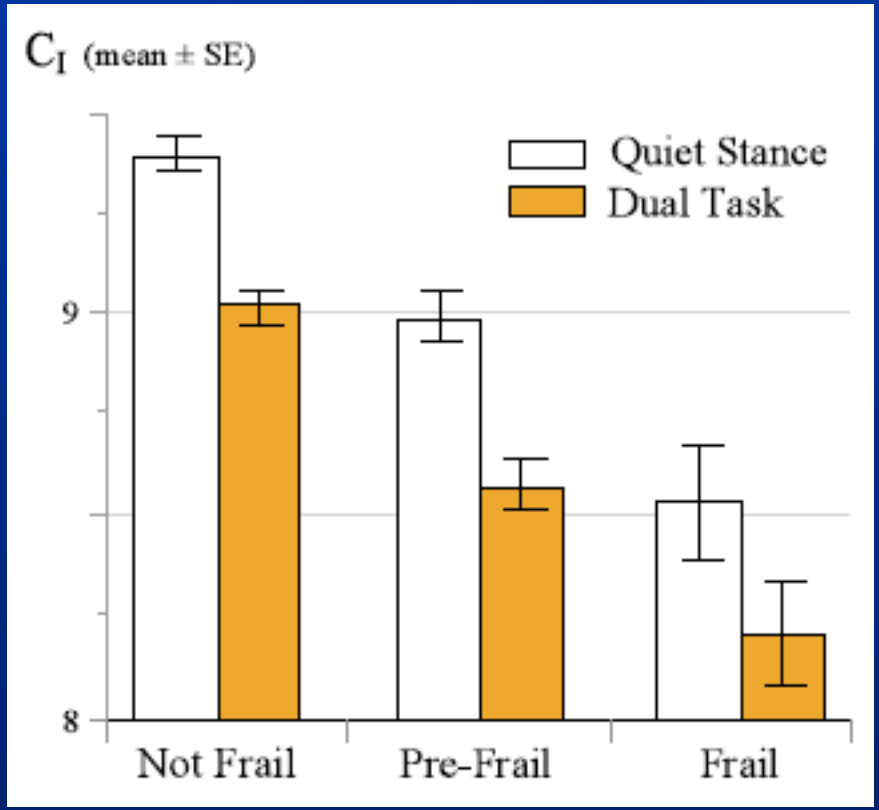

Multiscale entropy analysis
Sample entropy
2
1.5
1
0.5
0
0
4
8
12
16
20
Scale factor
Original
Drended (IMFs 1 to 4)

Complexity Analysis of the Sway Time Series



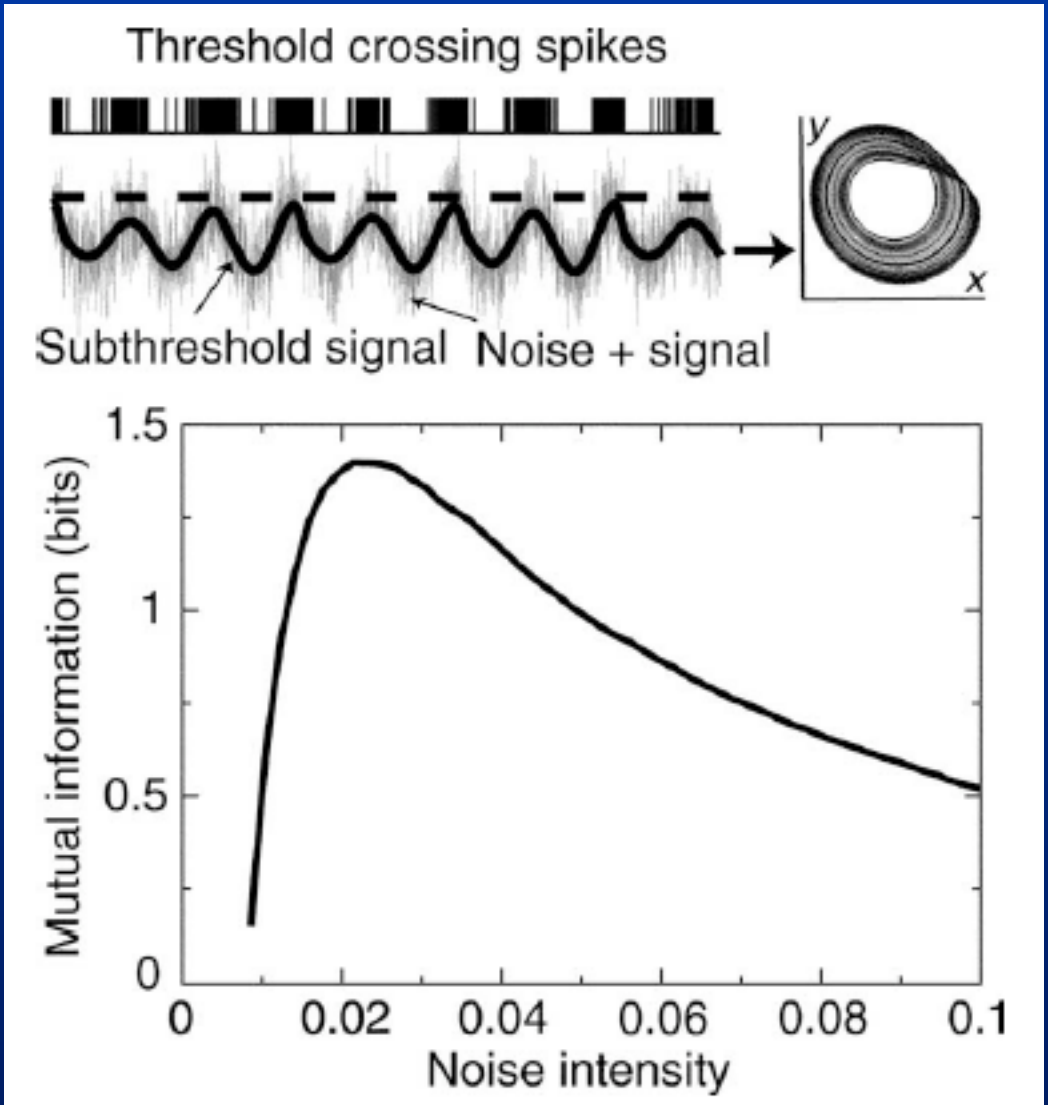
Complexity: young > elderly fallers
elderly non-fallers > fallers

Stress Reduces COP Complexity

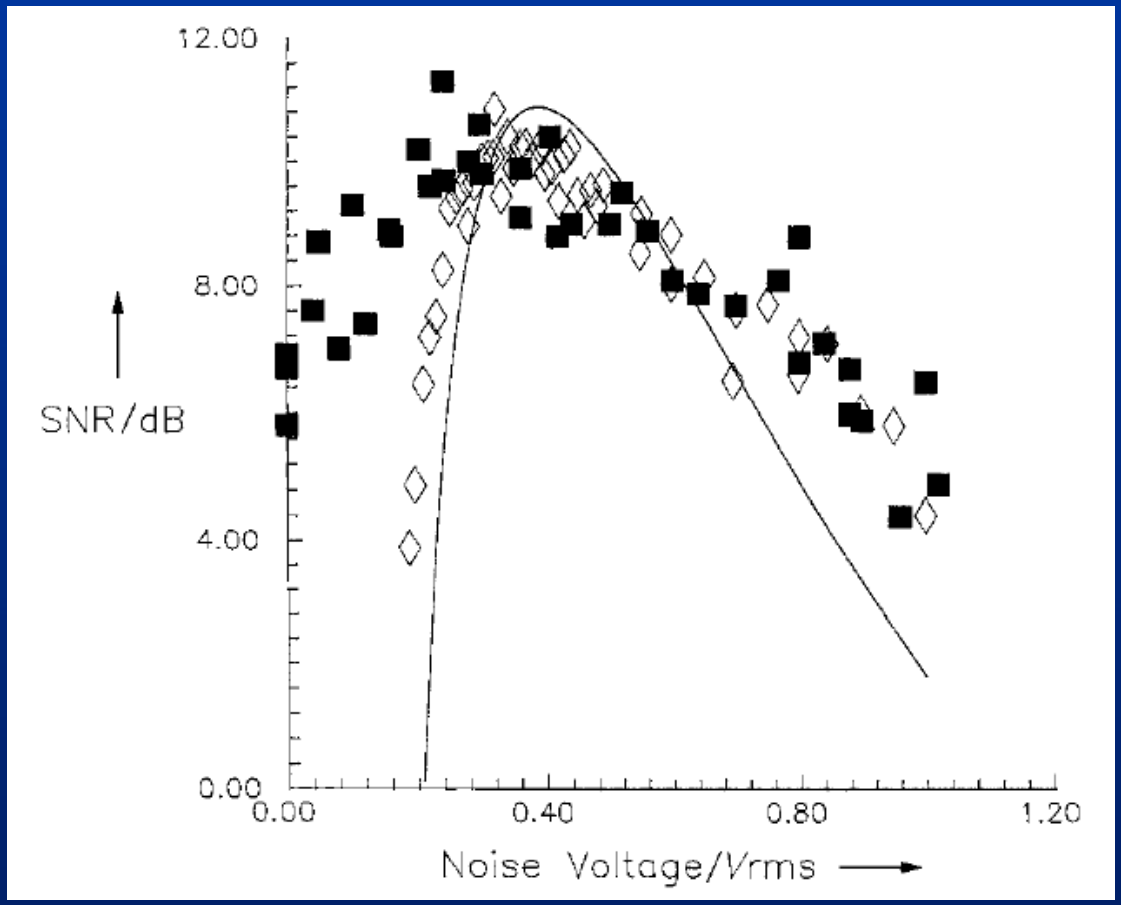


Kang *et al.* J Gerontol Med Sci 2009; **64**:1304-1311.

Stochastic Resonance



SR: crayfish vs. model



Douglas *et al.* Nature 1993; 365:337

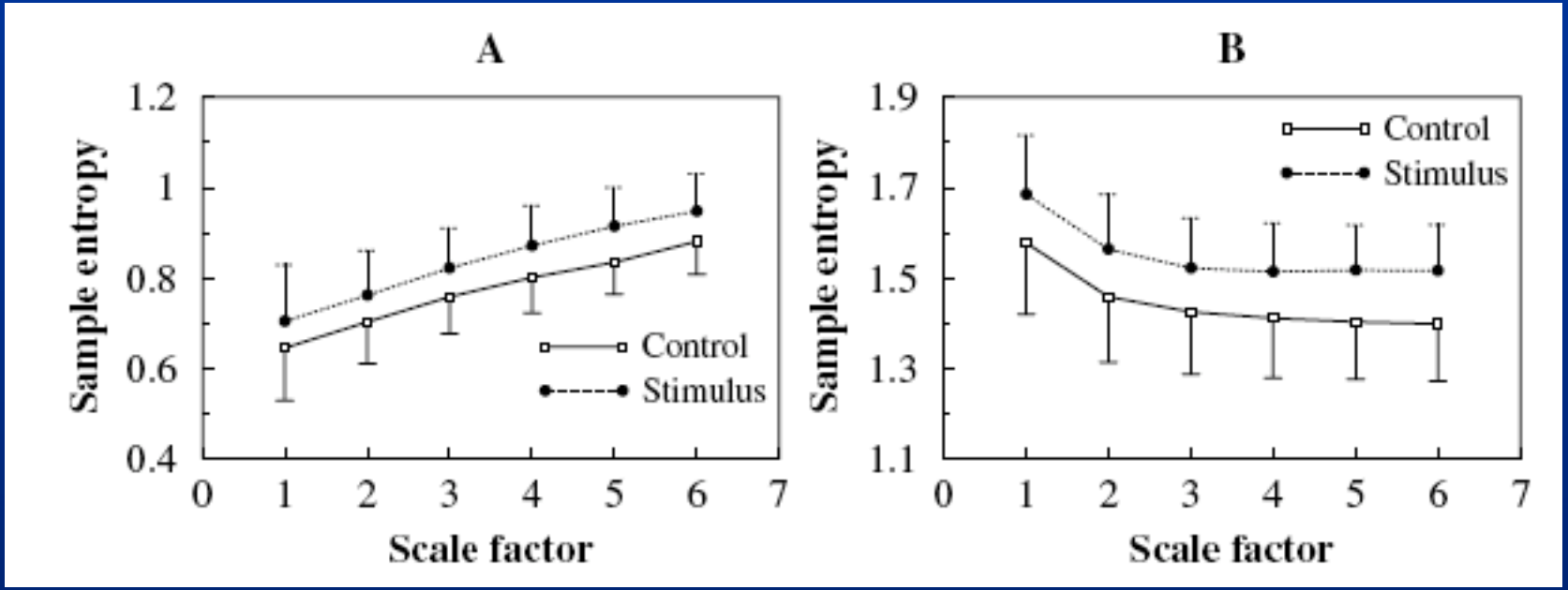
Stochastic Resonance

$\sigma = 10$ $\sigma = 90$ $\sigma = 300$

Simonotto *et al.* Phys Rev Lett 1997; 78:1186

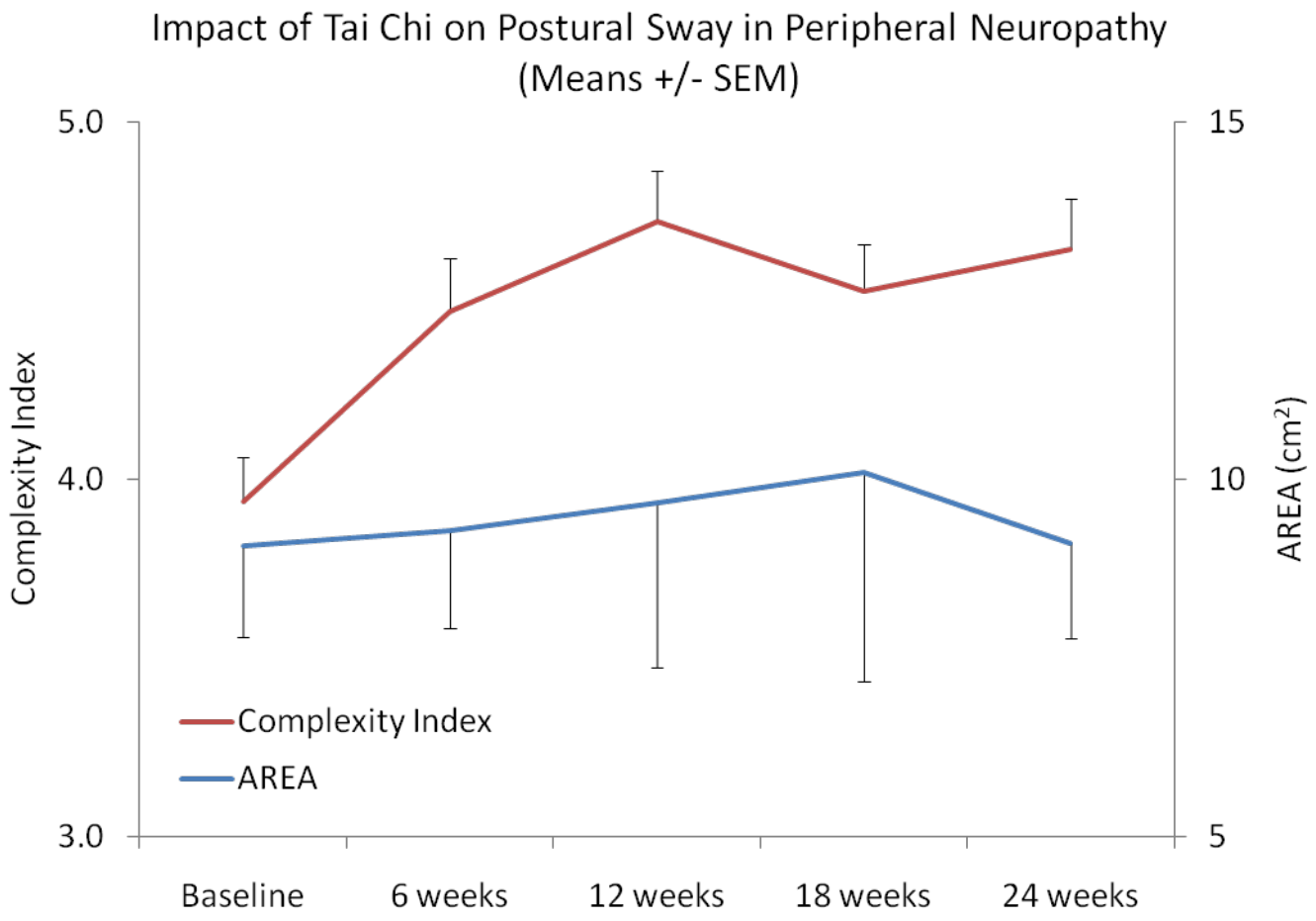
Sub-threshold Noise Increases Complexity of Sway Dynamics in Elderly (n=12)

One elderly subject (10 trials)

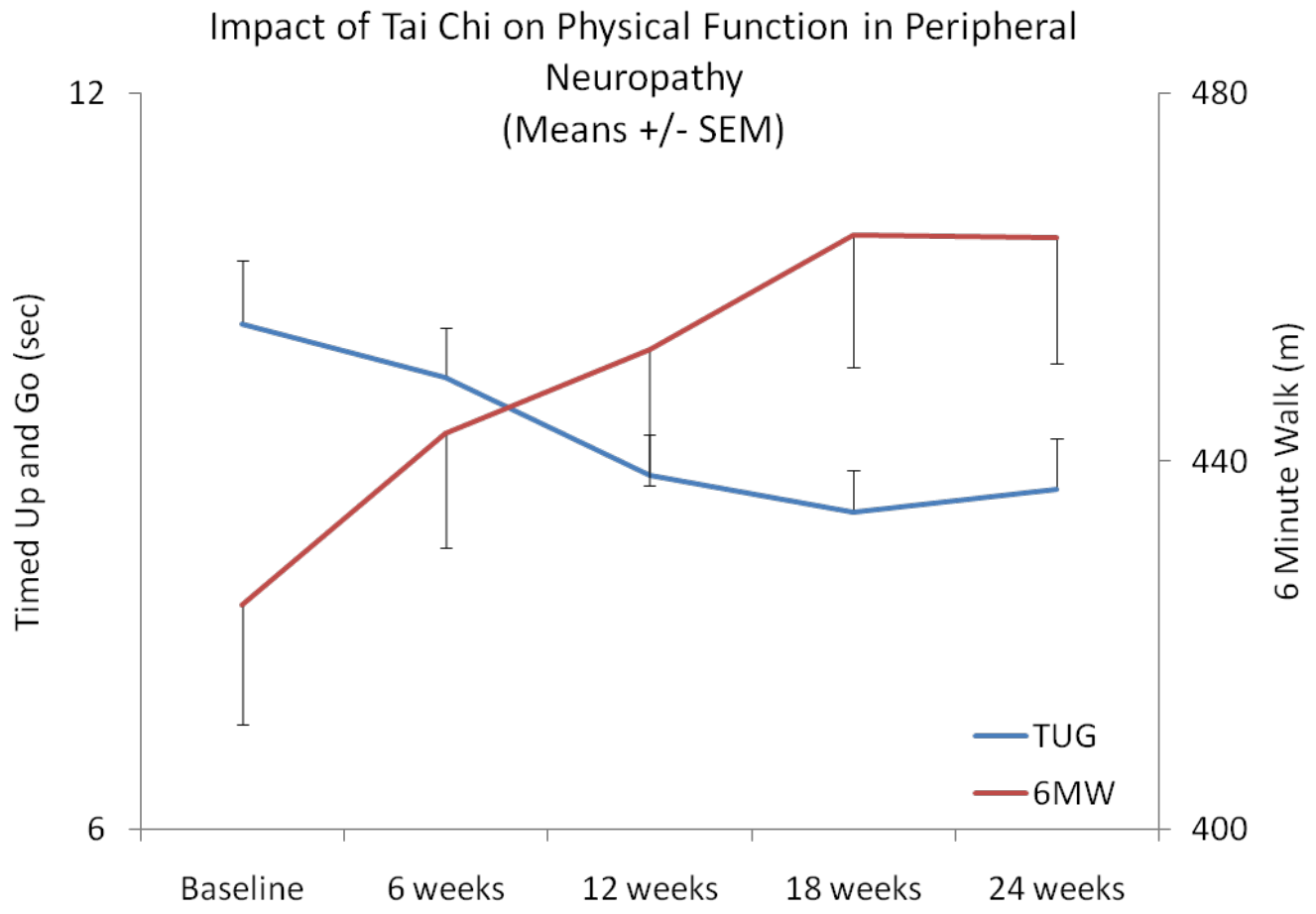


Complexity: input noise > control time series

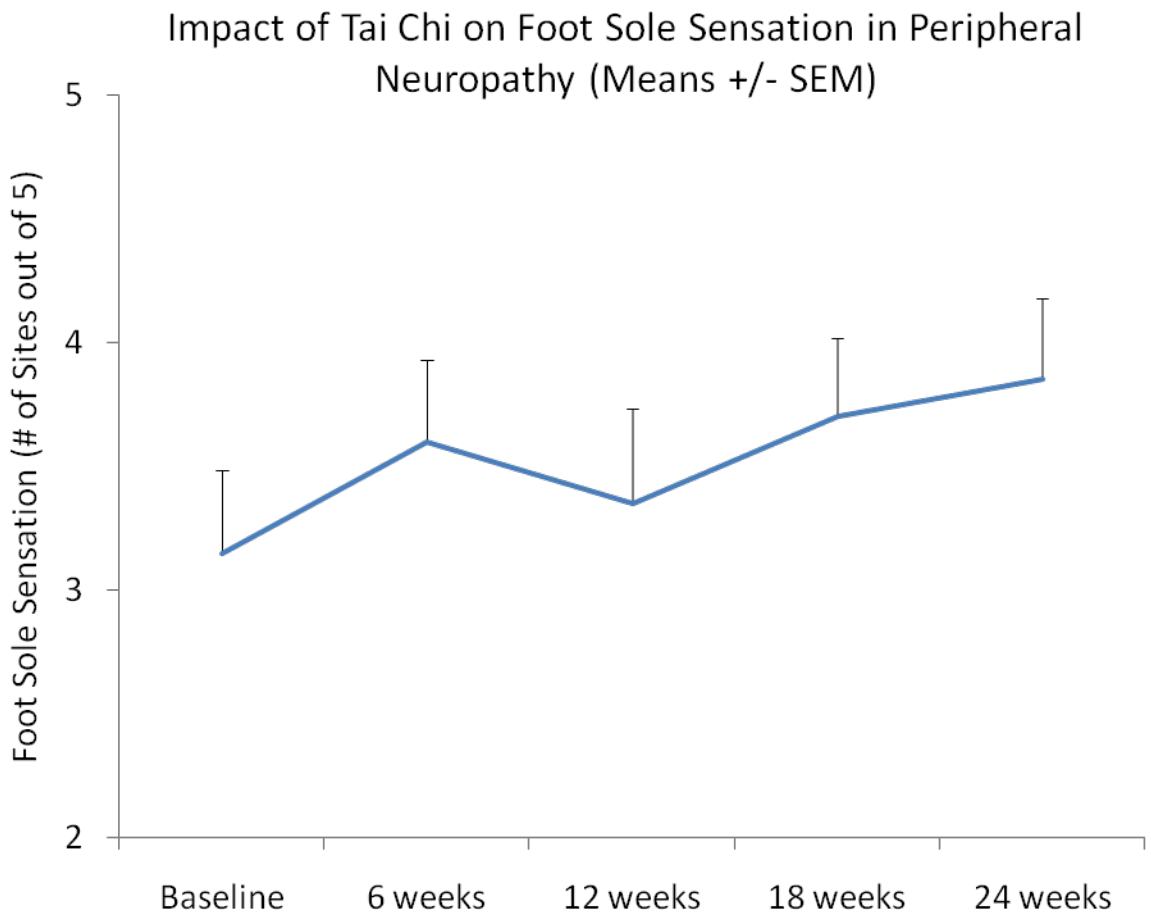
Costa *et al.* Europhysic Letters **77** 68008 (2007)

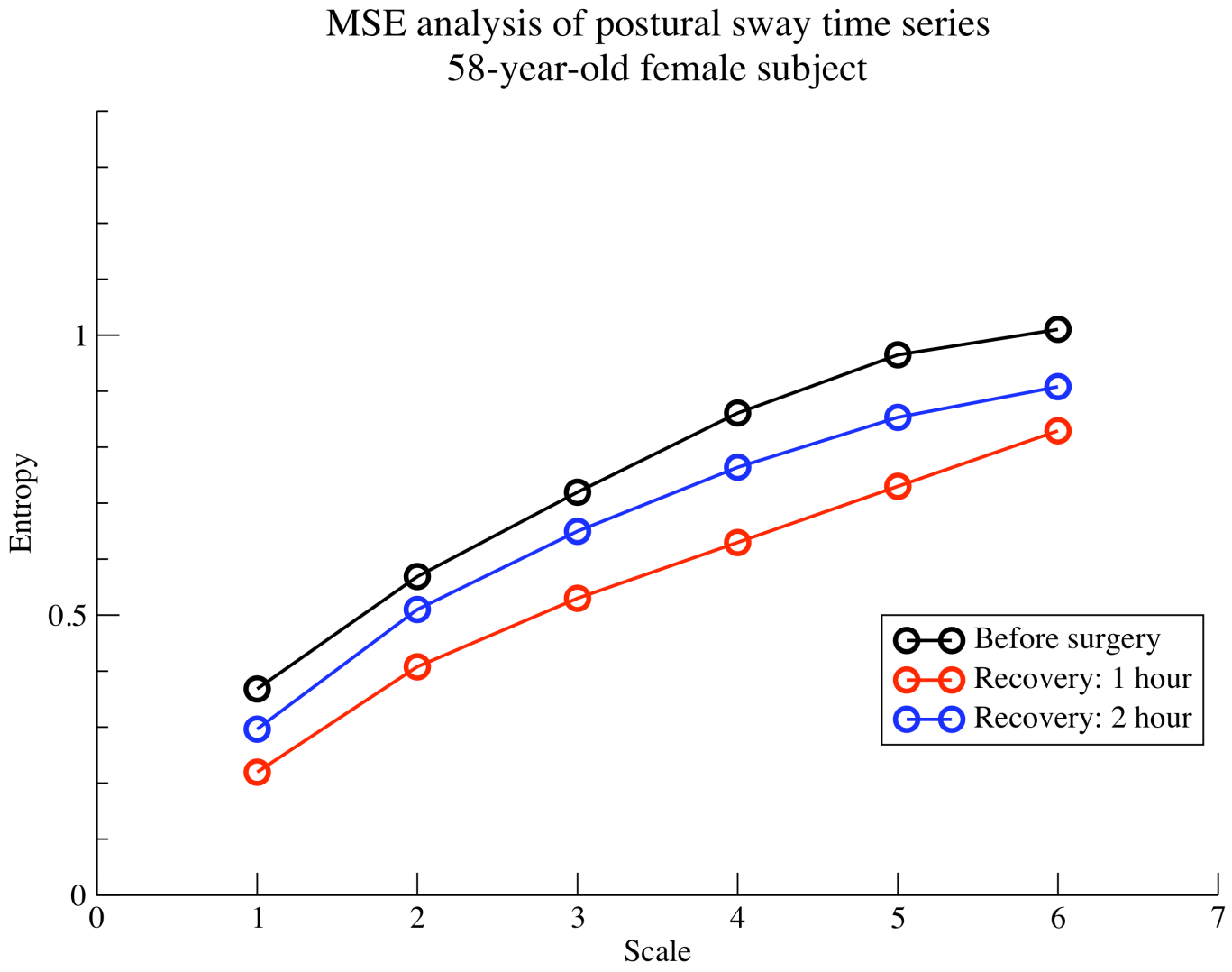


Dr. Brad Manor & Dr. Li Li @ LSU

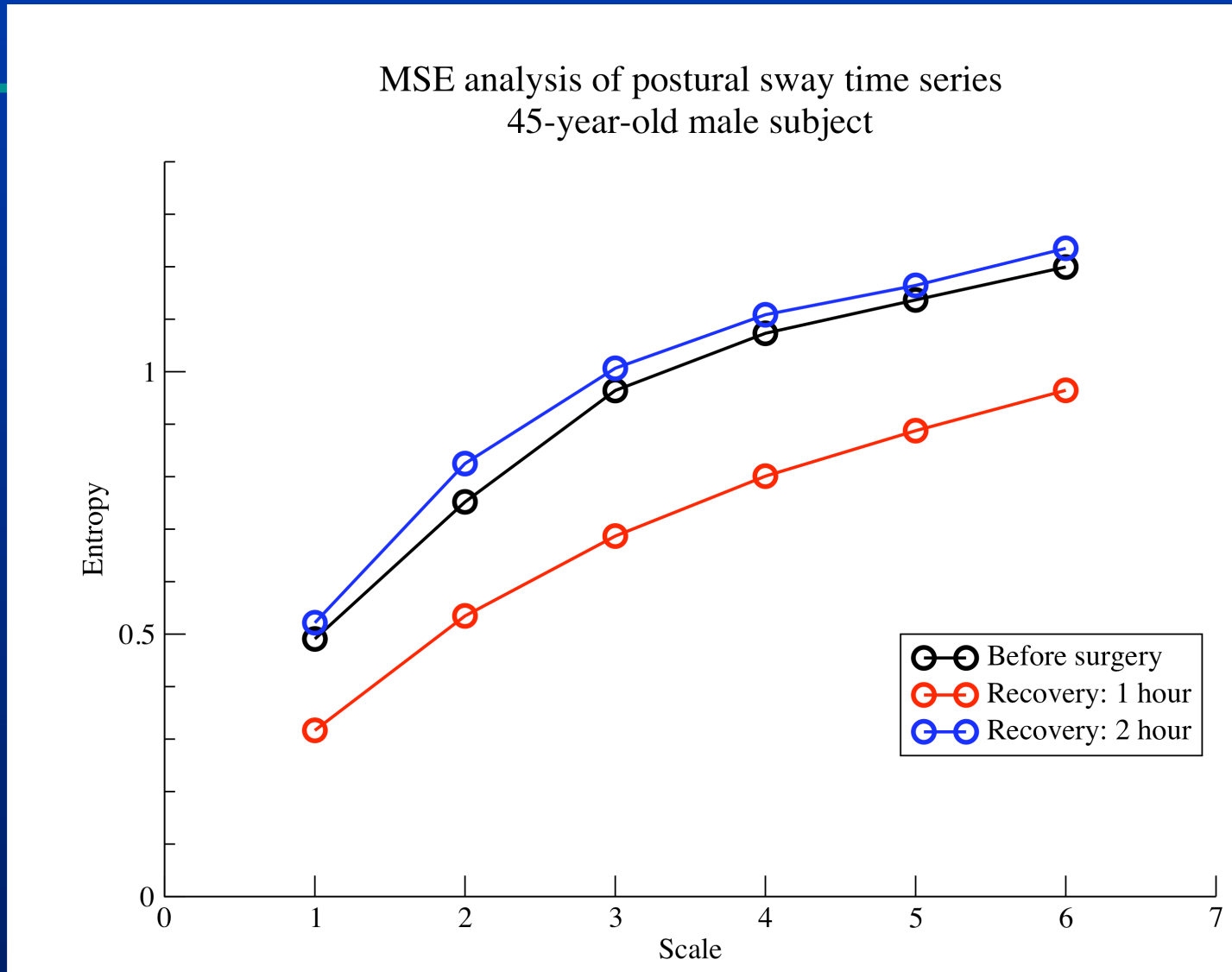


**Completing the timed up and go faster is better, and walking further in the 6 minute walk is better


Impact of Tai Chi on Foot Sole Sensation in Peripheral Neuropathy (Means +/- SEM)
Foot Sole Sensation (# of Sites out of 5)
5
4
3
2
Baseline
6 weeks
12 weeks
18 weeks
24 weeks



Fan *et al.* National Taiwan University Hospital



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