

Developing Dynamical Indicators of Resilience Based on Physiologic Time Series in Older Adults

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Quantifying resilience

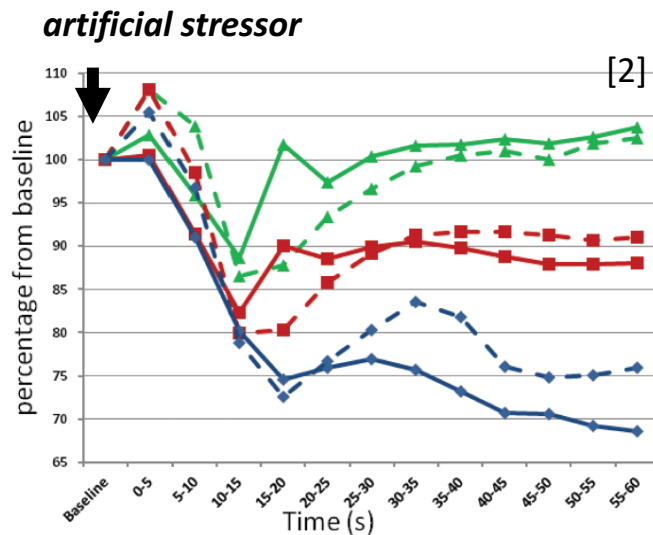
- Predict how patients will recover when health is challenged by disease or treatment
- Physical resilience = an individual's ability to **resist** functional decline or **recover** physical health following a stressor [1]
- Dynamical phenomena require dynamic tests
- Complement static indicators of reserve capacities or cumulative damage

Dynamical measurements

Two types:

- 1) Challenge test: perturb the body and measure recovery time

*Orthostatic
challenge test*

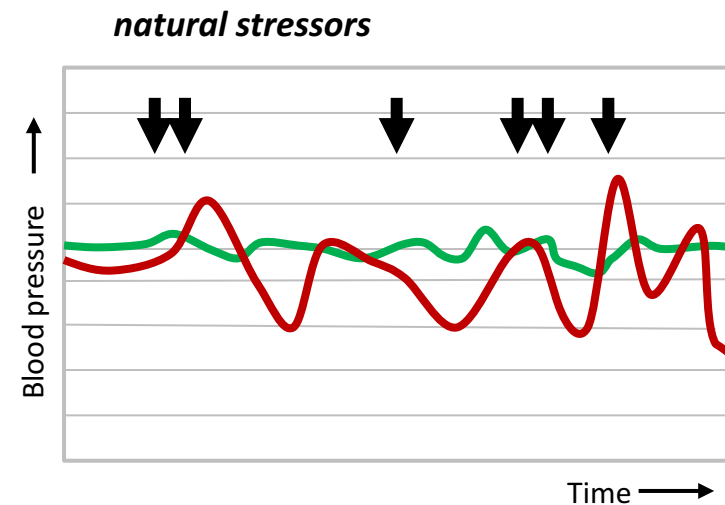
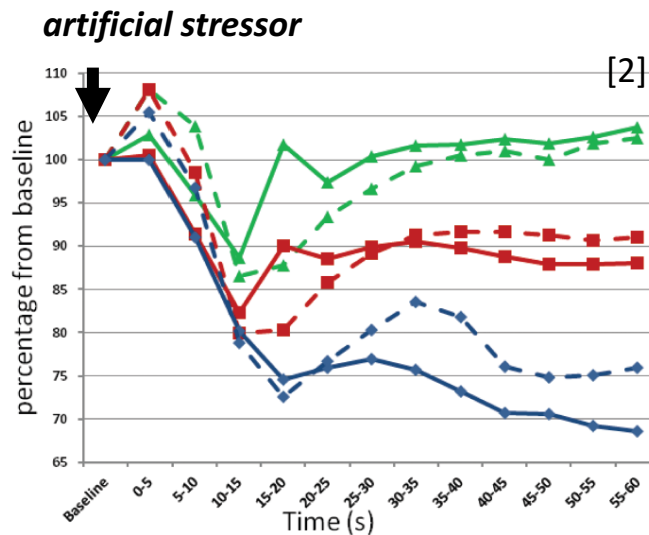


Dynamical measurements

Two types:

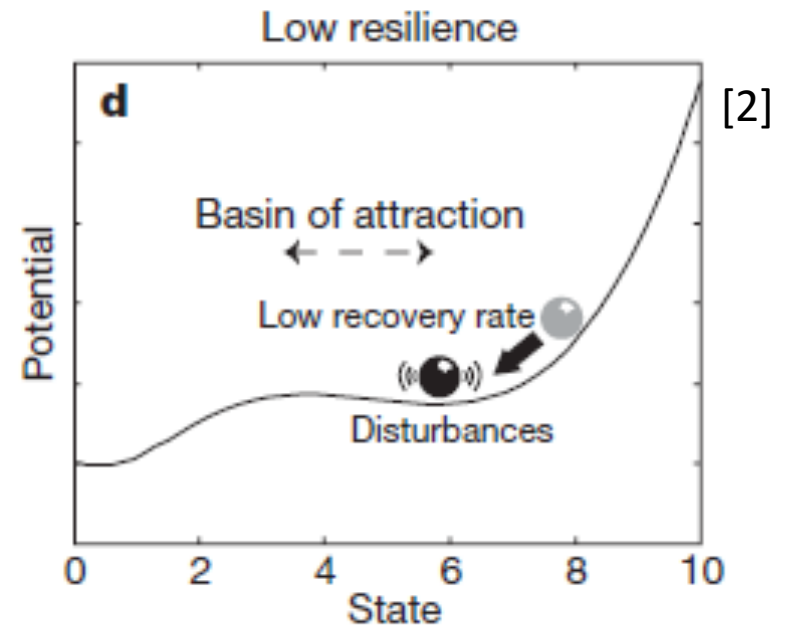
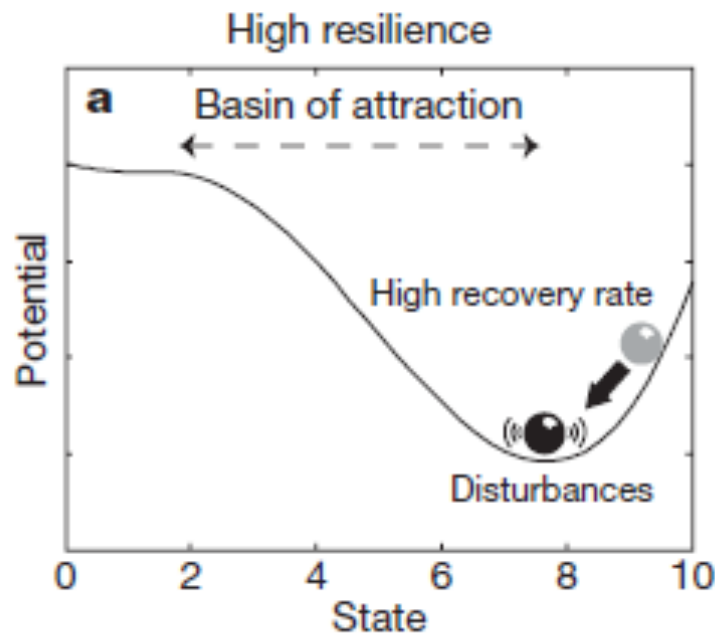
- 1) Challenge test: perturb the body and measure recovery time
- 2) Monitoring of *natural* perturbations: zoom in on “microdynamics”

Orthostatic
challenge test



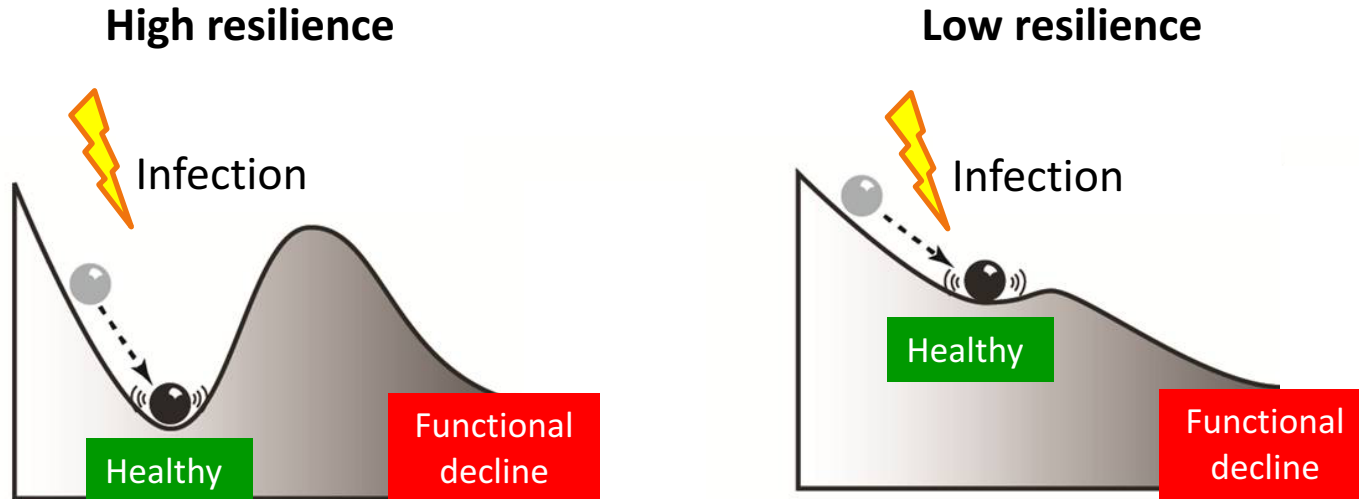
Low resilience → critical slowing down

- Generic theory of dynamical systems [3]
- Rate of change around the **equilibrium** decreases
- Changes in pattern of fluctuations of parameters over time



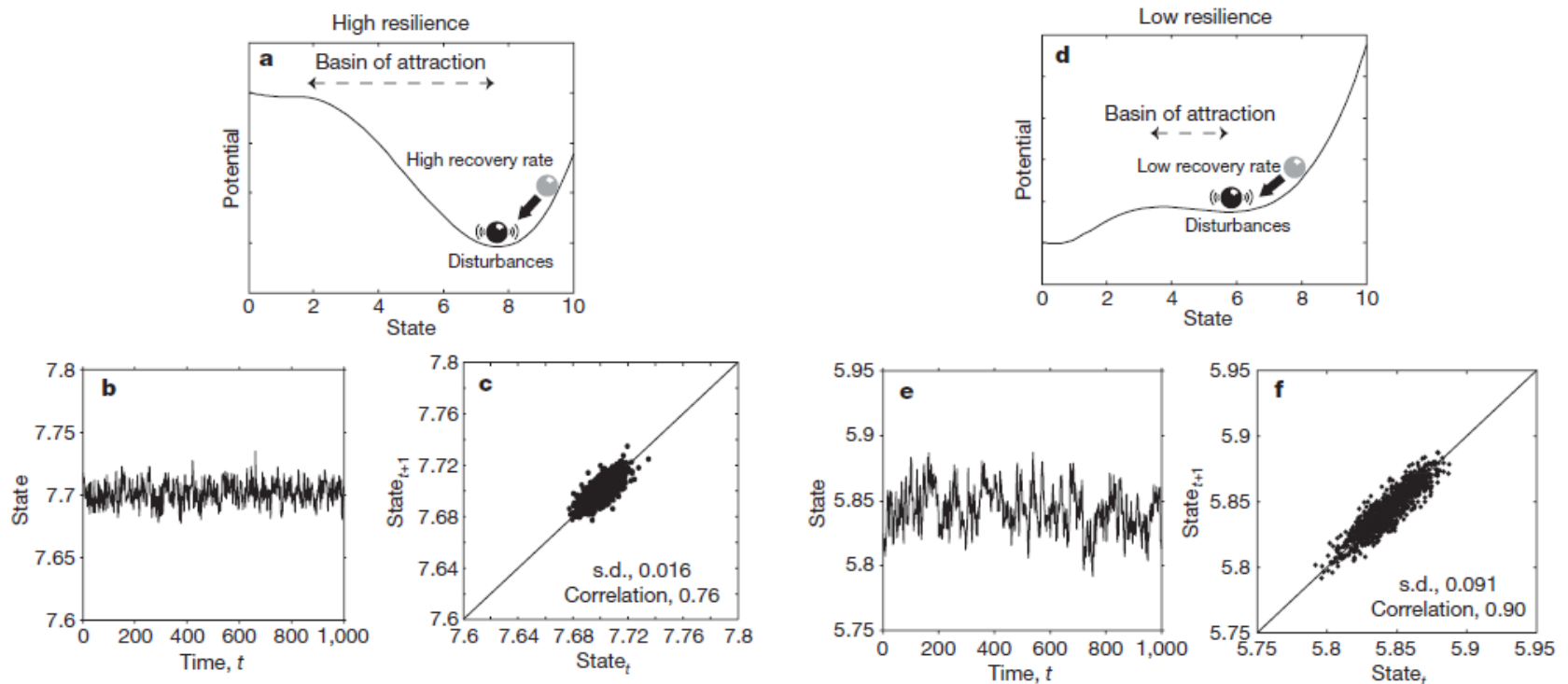
Low resilience → critical slowing down

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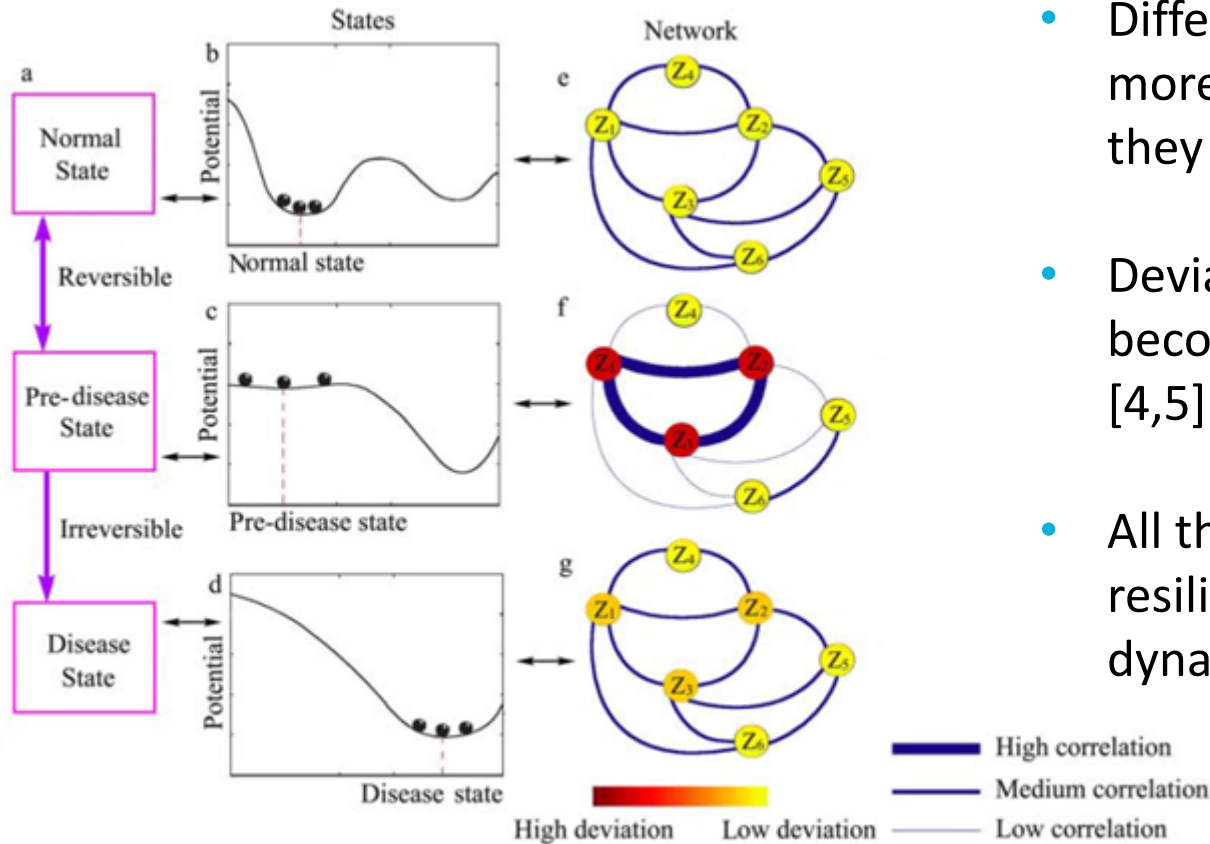


Dynamical indicators of resilience (1+2)

Critical slowing down typically causes an **increase in variance + temporal autocorrelation** of fluctuations of a parameter measured over time [3]



Dynamical indicators of resilience (3)



- Different subsystems become more mutually dependent as they lose resilience
- Deviations of parameters become **more cross-correlated** [4,5]
- All three indicators of resilience evidenced in mood dynamics [6,7]

DIORs in the older person

Mood [6]

Critical slowing down as early warning for the onset and termination of depression

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Self-rated health [8]



Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2017, Vol. 72, No. 7, 991–996
doi:10.1093/gerona/glx065
Advance Access publication May 5, 2017



Research Article

Dynamical Resilience Indicators in Time Series of Self-Rated Health Correspond to Frailty Levels in Older Adults

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Postural balance [9]



Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2018, Vol. XX, No. XX, 1–8
doi:10.1093/gerona/gly170
Advance Access publication July 25, 2018



Research Article

Dynamical Indicators of Resilience in Postural Balance Time Series Are Related to Successful Aging in High-Functioning Older Adults

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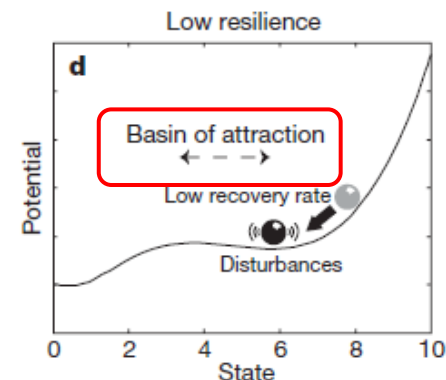
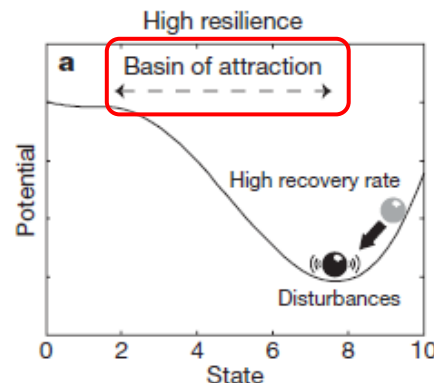
²Department of Environmental Sciences, Wageningen University, the Netherlands. ³Department of Rehabilitation, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, the Netherlands. ⁴Department of Physiology, Radboud University Medical Center, Nijmegen, the Netherlands.

Collecting time series data for DIORs

Time-series measures showing short- and long- term fluctuations in levels of a given function

- Heart rate, blood pressure , balance [10]
 - Body temperature
 - Attention (reaction times)
- } **Physical**
- Self-rated mood / anxiety / wellbeing / health / fatigue → **Mental**

Keep the theory
in mind!

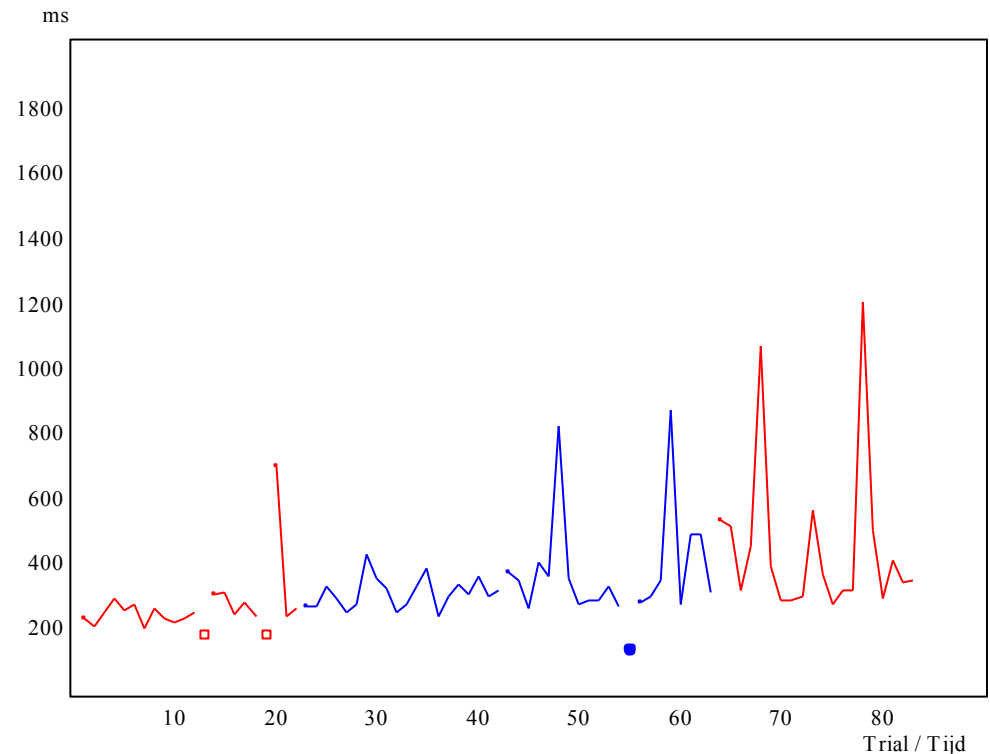


Example: reaction speed time series

80 trials in 5 minutes

Time series is a non-parametric distribution with large outliers

No clear equilibrium / basin of attraction!



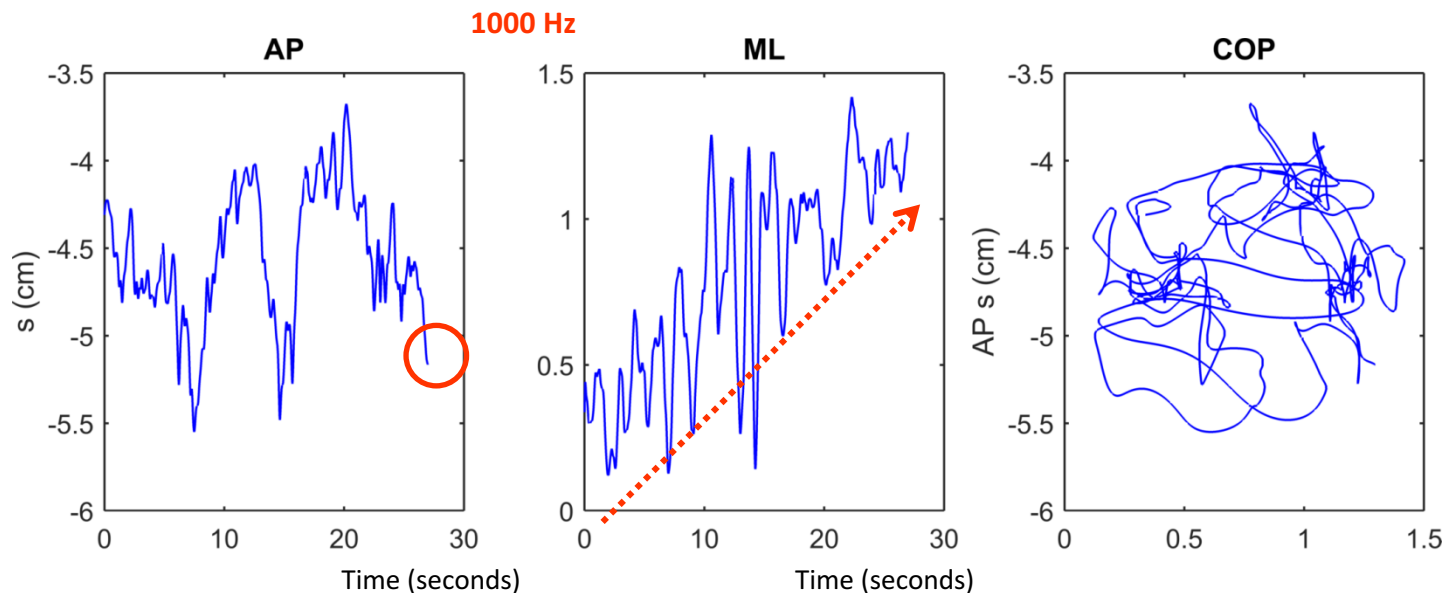
Analyzing time series data for DIORs

Main challenges

- Step 1: Exploration of time series
 - Visualize data with plots
 - Data in context of system and responses of interest
- Step 2: Pre-processing of data: filtering, smoothing, detrending, etc.
 - Driven by knowledge of the system of interest
 - Driven by the data
- Step 3: Calculation of DIORs
 - Variance: standard deviation
 - Temporal autocorrelation: choose a lag?
 - Cross-correlation: Pearson's correlation
- Step 4: Analyze relationship with relevant participant characteristics

Analyzing DIORs in time series

- Step 1: Exploration of time series
 - Visualize data with plots
 - Data in context of system and responses of interest



Max. 3 Hz



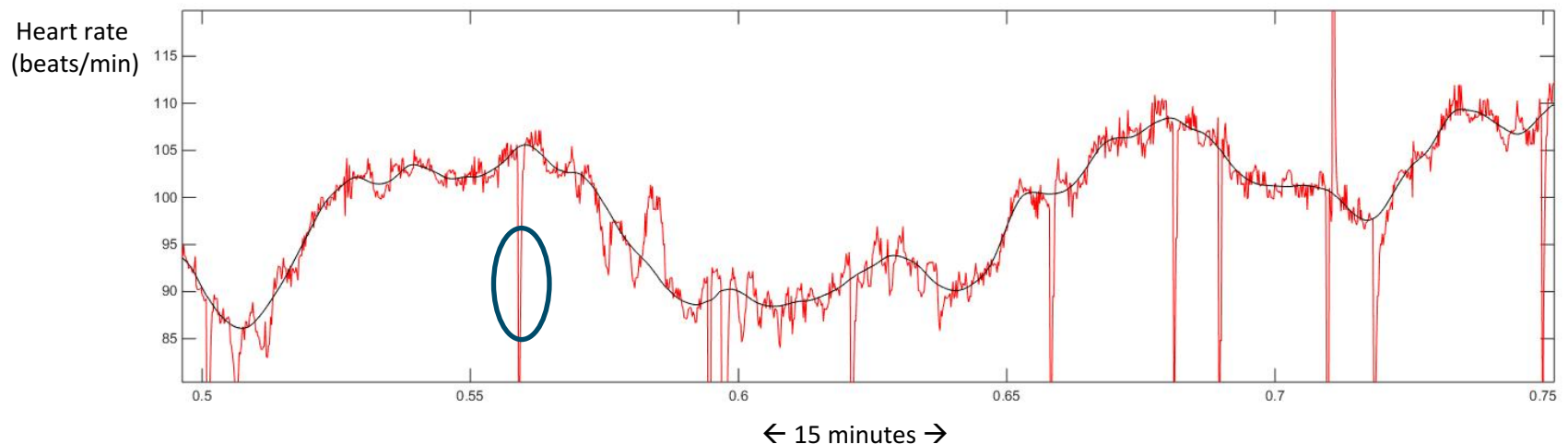
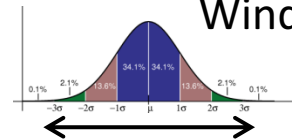
Analyzing DIORs in time series

- Step 2: Pre-processing of data: filtering, **smoothing**, detrending, etc.
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Smoothing function

- Moving average
- Gaussian kernel
- LOESS

Window size? → visual inspection

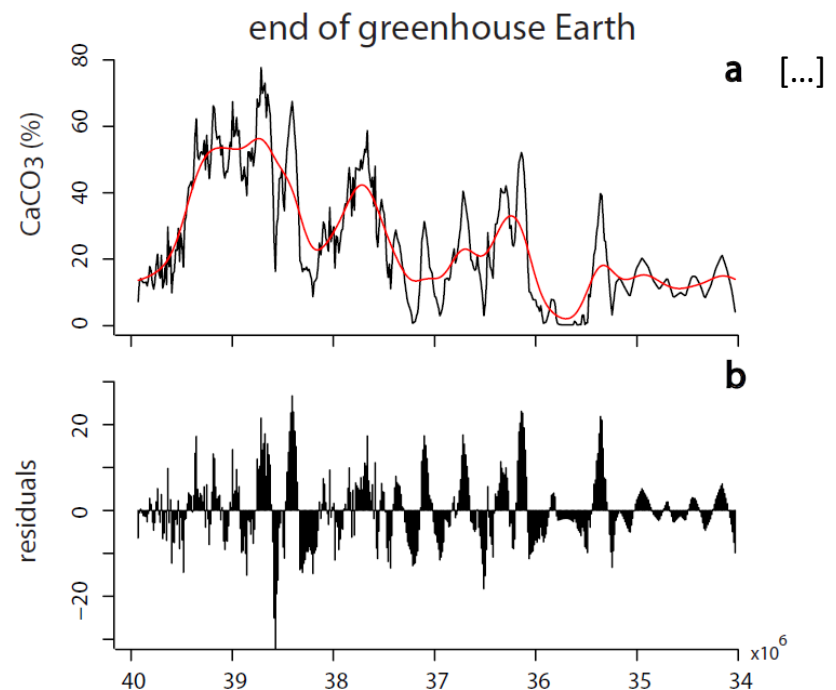
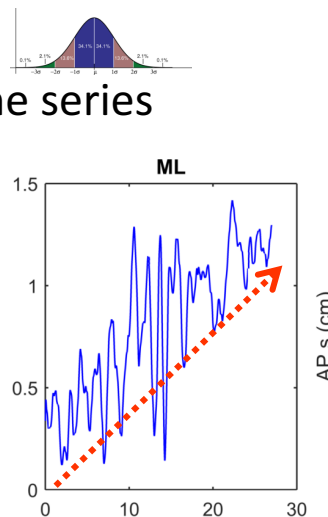


Analyzing DIORs in time series

- Step 2: Pre-processing of data: filtering, smoothing, **detrending**, etc.
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Detrending

- Choose smoothing function
- Choose window size
- Subtract smooth time series
- Work with residuals

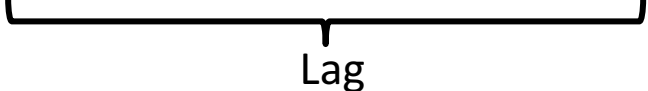


Analyzing DIORs in time series

- Step 3: Calculation of DIORs
 - Variance: standard deviation
 - Temporal autocorrelation: choose a lag
 - Cross-correlation: Pearson's correlation

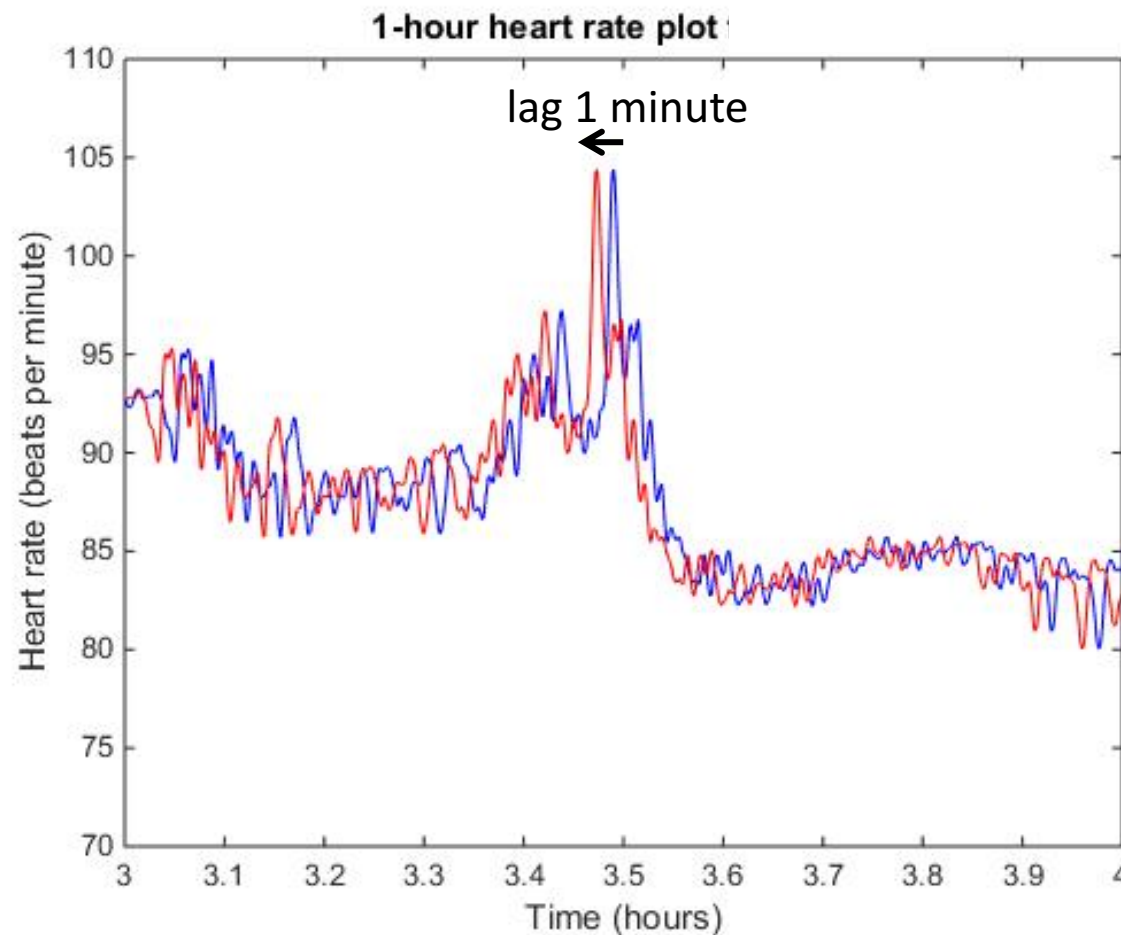
Choosing a lag for oversampled time series

-Shift the time series a certain number of data points

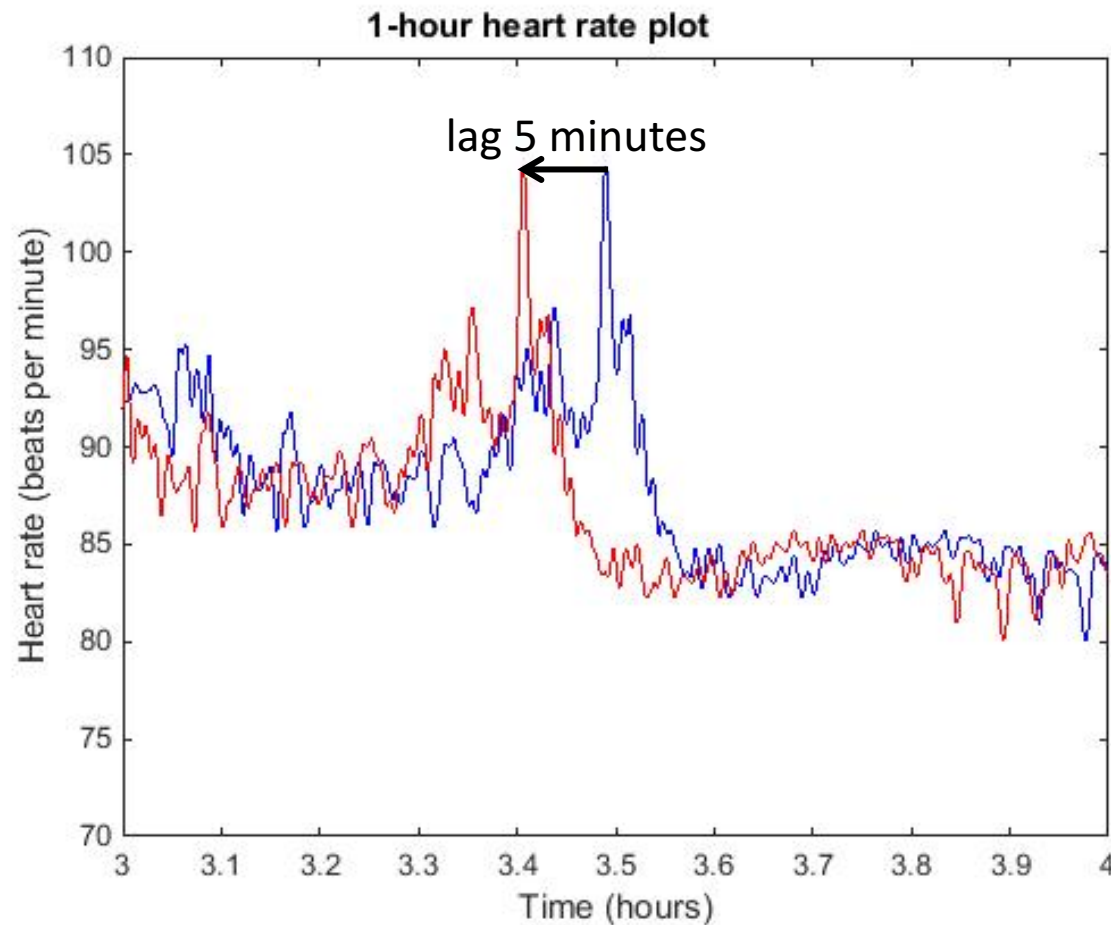


Lag

Example: heart rate temporal autocorrelation

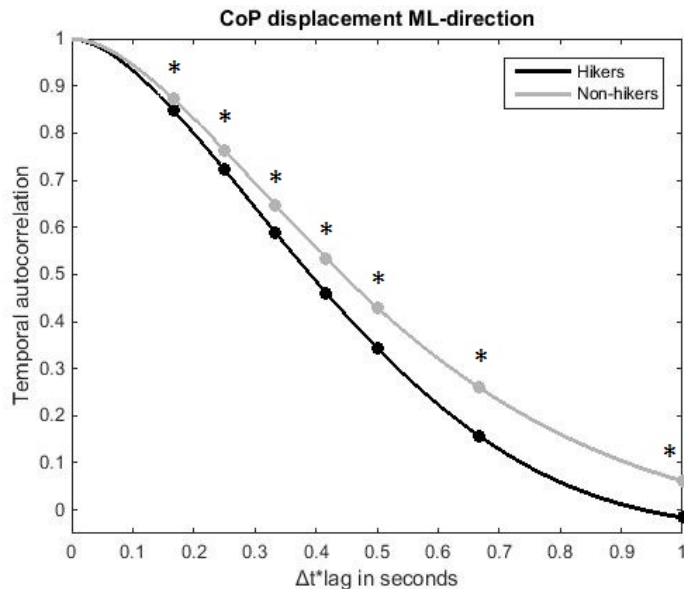


Example: heart rate temporal autocorrelation



Analyzing DIORs in time series

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Choosing a lag for oversampled time series

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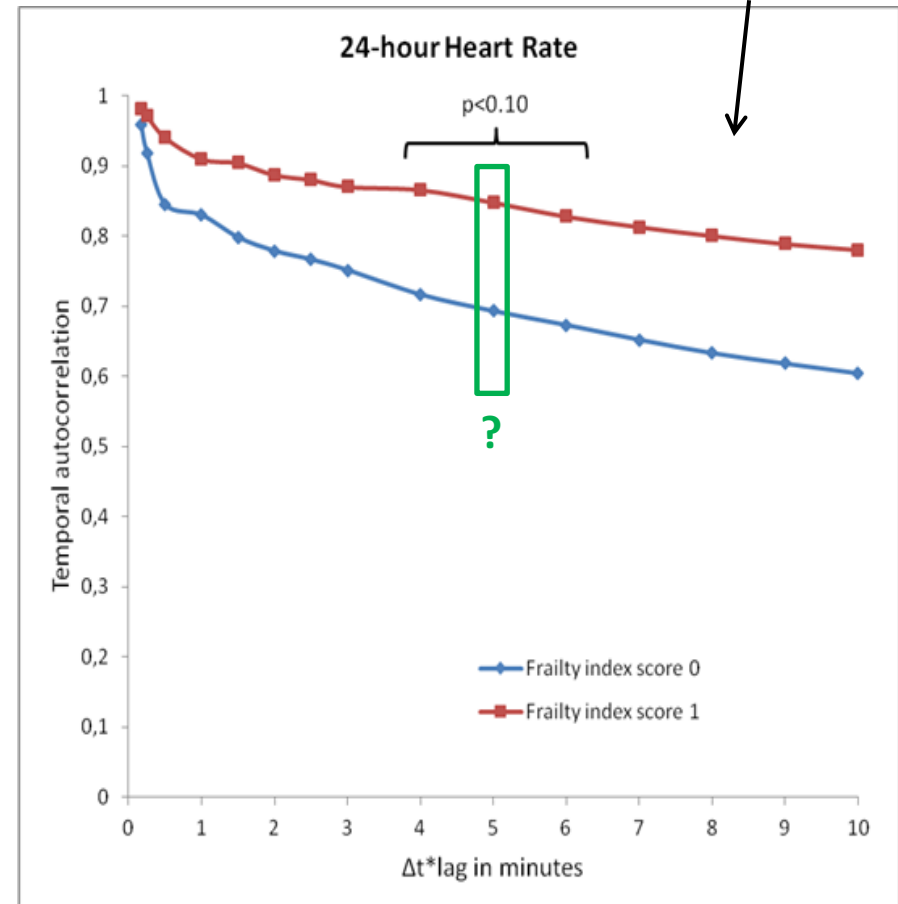
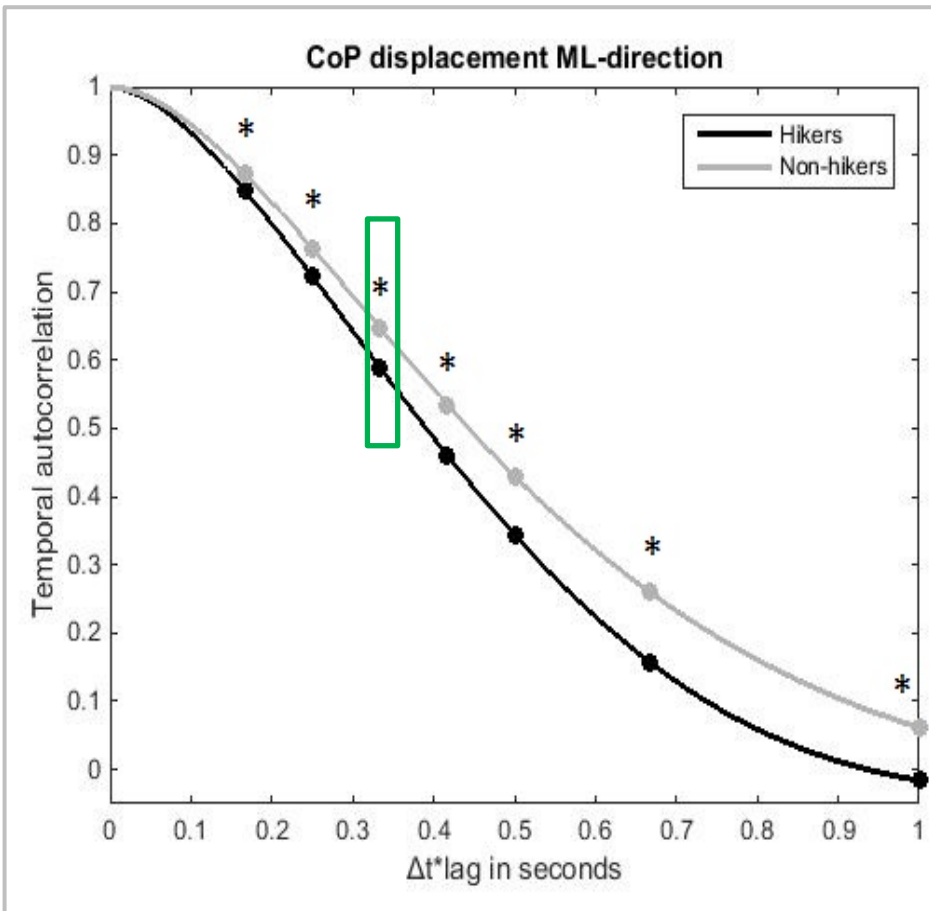
Lag

-What is the characteristic response rate of the system?

-Within the range of interest, compare multiple lags with an autocorrelation function graph

Example: temporal autocorrelation graphs

Preliminary results!



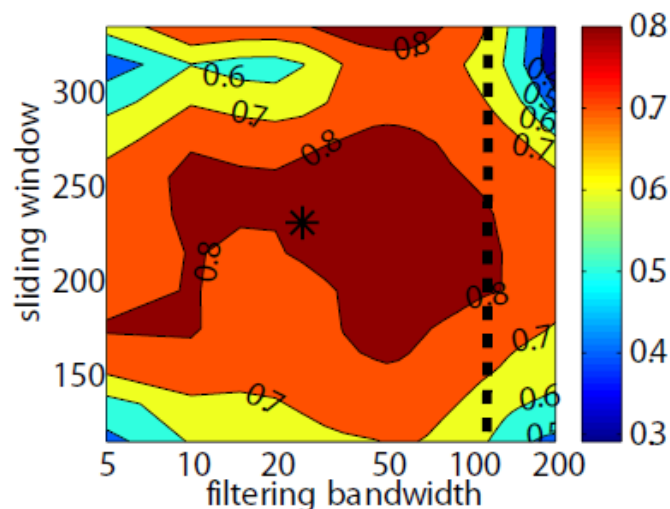
Analyzing DIORs in time series

Step 2: Pre-processing of data: filtering, smoothing, detrending, etc.

- Driven by knowledge of the system of interest
- Driven by the data

Step 3: Calculation of DIORs

- Variance: standard deviation
- Temporal autocorrelation: choose a lag
- Cross-correlation: Pearson's correlation



← Combine parameters in a contour plot with a test statistic?

Analyzing DIORs in time series

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- Step 4: Analyze relationship with relevant participant characteristics

Crucial considerations to make beforehand

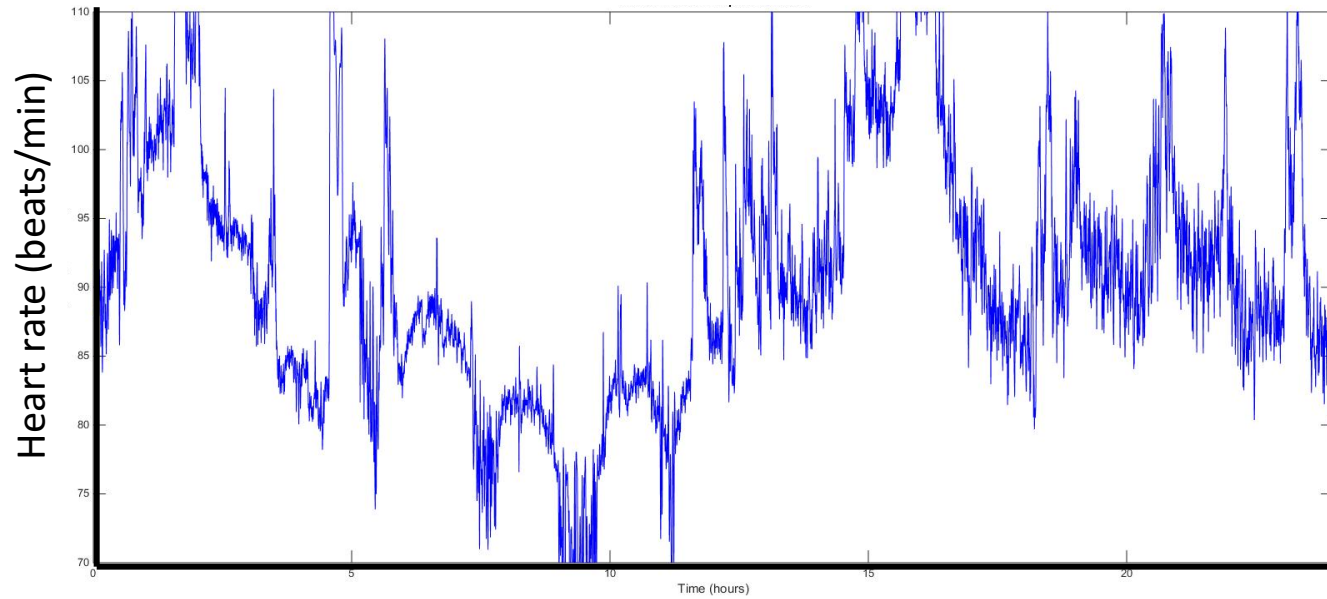
- What exactly is the **system** and the **response of interest**?
- Do your measurements capture the characteristic system dynamics?
 - Which variable(s)?
 - Which measurement device/study design?
 - Occurrence of natural perturbations?
- Frequency of observations: sampling at intervals shorter than the characteristic time scales of the slowest return rate of the system

Interpretation of results

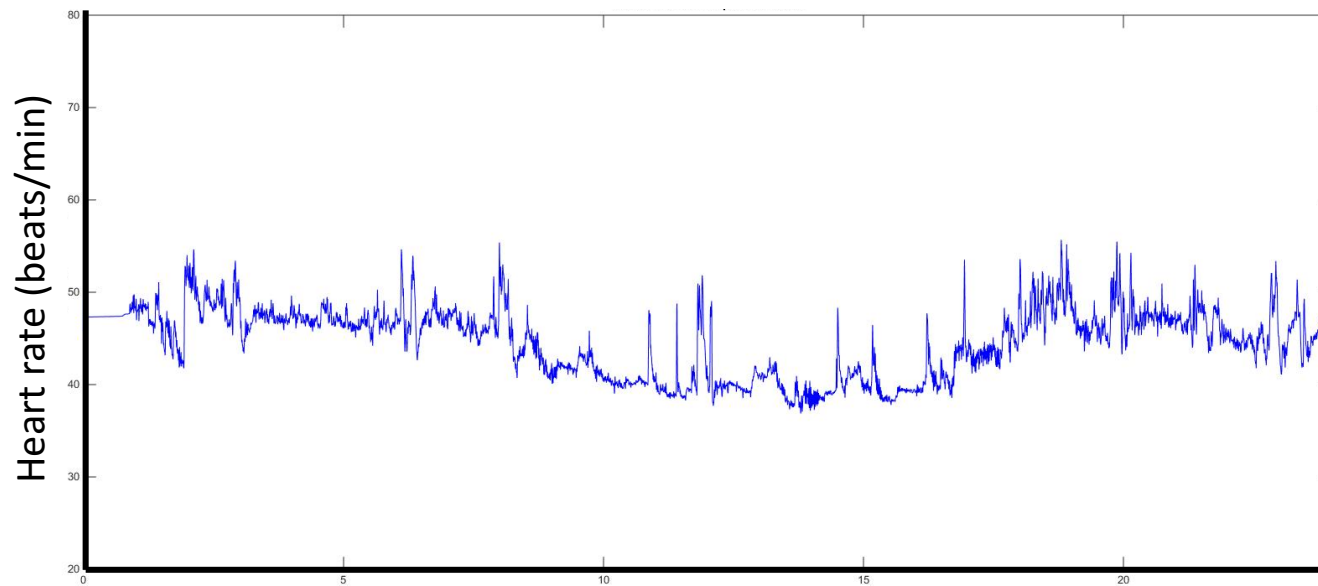
Main challenges:

1. Enormous heterogeneity of geriatric patients
 - Clinical trajectories
 - **Dynamic fluctuations of bodily functions**

Examples



Large fluctuations

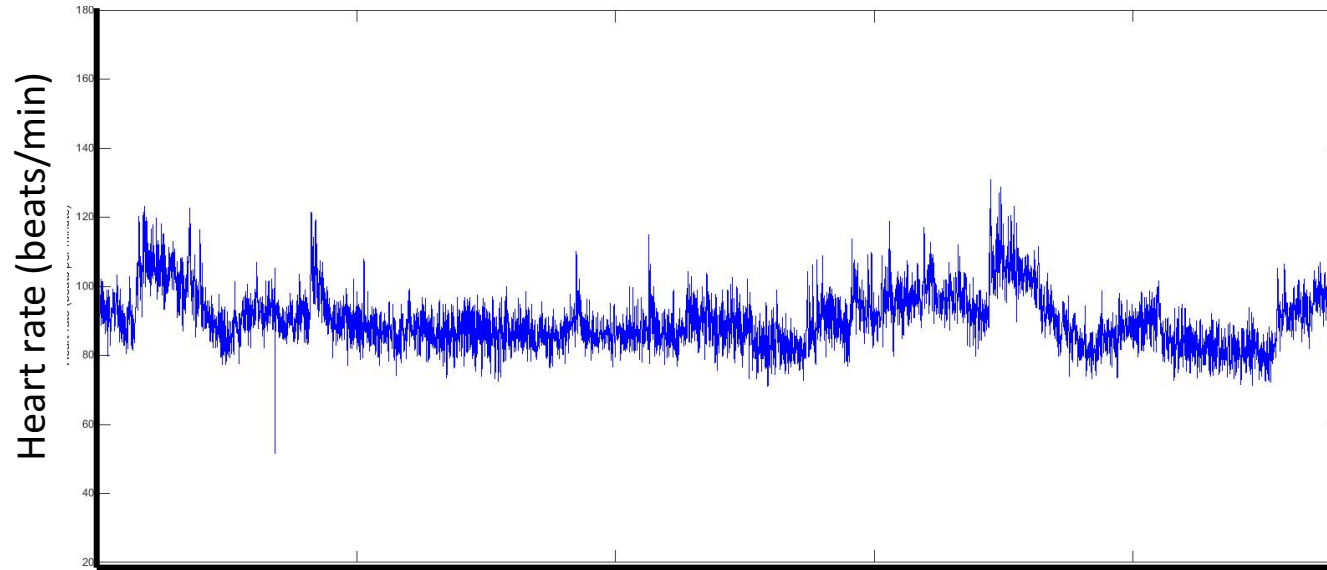


Small fluctuations

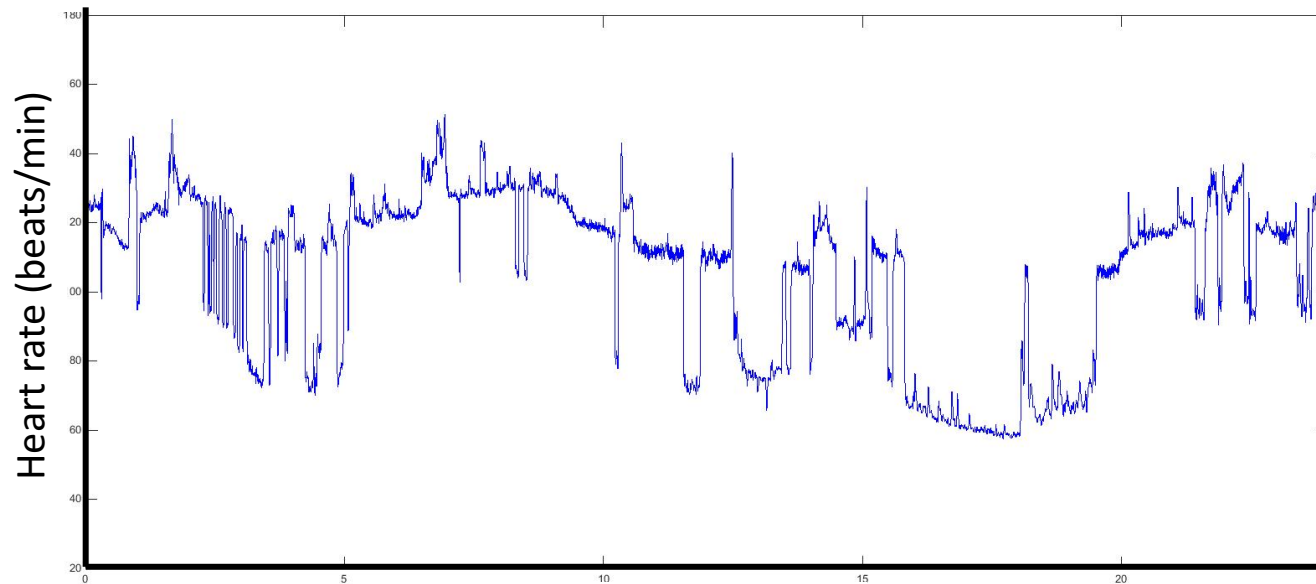
← 24 hours →

Zoomed out

Examples



Atrial fibrillation



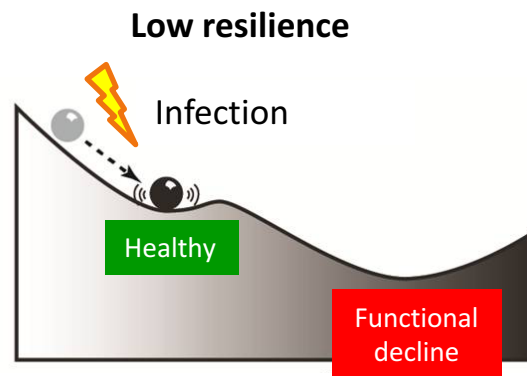
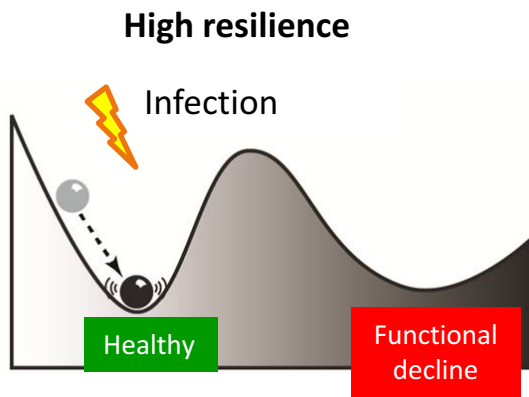
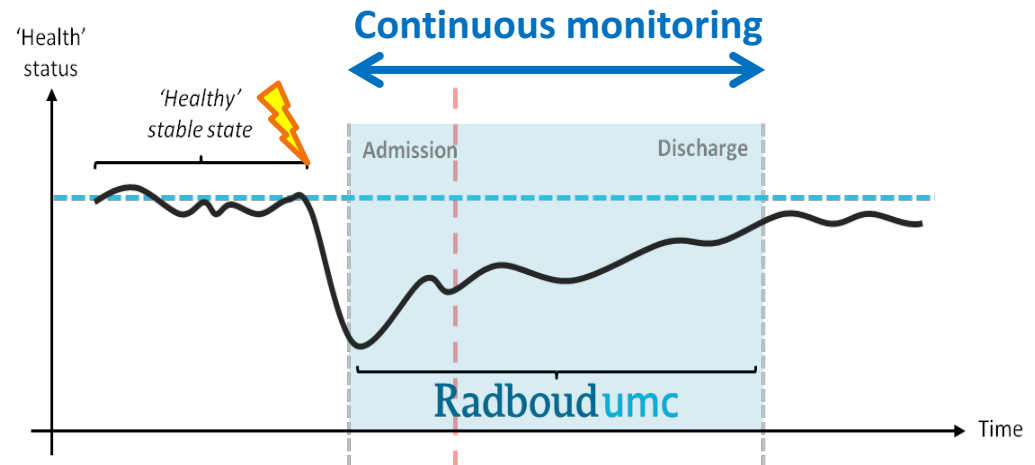
Sudden transitions
In heart rhythm

← 24 hours →

Interpretation of results

Main challenges:

1. Enormous heterogeneity of geriatric patients
2. Results in context of theory of critical slowing down



Discussion

- Preliminary evidence for the value of dynamical indicators of resilience in the aging human
- Challenge to collect&analyze data and interpret results
- How are DIORs related to other complexity measures?
- Which systems are the right proxies for resilience of the whole body?
- How to study resilience from the perspective of the network of organs (cross-correlations)?

References

1. Whitson HE, Duan-Porter W, Schmader KE, Morey MC, Cohen HJ, Colón-Emeric CS. Physical resilience in older adults: Systematic review and development of an emerging construct. *J Gerontol A Biol Sci Med Sci*. 2016;71:489–495.
2. Lagro J, et al. Impaired systolic blood pressure recovery directly after standing predicts mortality in older falls clinic patients. *J Gerontol A Biol Sci Med Sci*. 2014 Apr;69(4):471-8.
3. Scheffer M, Bascompte J, Brock WA, et al. Early-warning signals for critical transitions. *Nature*. 2009;461:53–59.
4. Chen L, Liu R, Liu ZP, Li M, Aihara K. Detecting early-warning signals for sudden deterioration of complex diseases by dynamical network biomarkers. *Sci Rep*. 2012;2:342.
5. Dakos V, van Nes EH, Donangelo R, Fort H, Scheffer M. Spatial correlation as leading indicator of catastrophic shifts. *Theor Ecol*. 2010;3:163–174.
6. van de Leemput IA, et al. Critical slowing down as early warning for the onset and termination of depression. *Proc Natl Acad Sci USA*. 2014;111:87–92.
7. Wichers M, Groot PC; Psychosystems, ESM Group, EWS Group. Critical slowing down as a personalized early warning signal for depression. *Psychother Psychosom*. 2016;85:114–116.
8. Gijzel SMW, van de Leemput IA, Scheffer M, Roppolo M, Olde Rikkert MGM, Melis RJF. Dynamical resilience indicators in time series of self-rated health correspond to frailty levels in older adults. *J Gerontol A Biol Sci Med Sci*. 2017;72:991–996.
9. Gijzel SMW, et al. Dynamical indicators of resilience in postural balance time series are related to successful aging in high-functioning older adults. *J Gerontol A Biol Sci Med Sci* 2018 [Epub ahead of print]
10. Hadley EC, Kuchel GA, Newman AB; Workshop Speakers and Participants. Report: NIA workshop on measures of physiologic resiliencies in human aging. *J Gerontol A Biol Sci Med Sci*. 2017;72:980–990.

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