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

[1] Whitson et al. 2015 JGMS
Dynamical measurements

Two types:

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

[2] Lagro et al. 2014 JGMS
Dynamical measurements

Two types:

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

2) Monitoring of *natural* perturbations: zoom in on “microdynamics”
Low resilience $\rightarrow$ 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

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

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

Self-rated health [8]

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

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Mood [6]

Postural balance [9]

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

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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)

- 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

- **Step 1**: Exploration of time series
  - \(\rightarrow\) Visualize data with plots
  - \(\rightarrow\) 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
  - \(\rightarrow\) Variance: standard deviation
  - \(\rightarrow\) Temporal autocorrelation: choose a lag?
  - \(\rightarrow\) Cross-correlation: Pearson’s correlation

- **Step 4**: Analyze relationship with relevant participant characteristics

Main challenges
Analyzing DIORs in time series

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

[Graph showing heart rate (beats/min) over time with annotations for smoothing functions and a highlighted section indicating a 15-minute timeframe]

Dakos et al. 2008 PNAS
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

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

[Graph showing detrending process]

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Dakos et al. 2008 PNAS
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
Example: heart rate temporal autocorrelation
Example: heart rate temporal autocorrelation
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
- 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!

Theory of DIORs – Data collection – Analysis – Results interpretation – Discussion
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

• **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 first
  → Cross-correlation: Pearson’s correlation

• **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
Heart rate (beats/min)

Examples

Large fluctuations

Small fluctuations

Radboudumc
Heart rate (beats/min)

Atrial fibrillation

Sudden transitions in heart rhythm
Interpretation of results

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

![Diagram showing healthy functional decline and adaptation to infection with high and low resilience.]
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


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