Statistical Methods for Online Monitoring in Intensive Care

Ursula Gather

joint work with

Matthias Borowski   Michael Imhoff   Silvia Kuhls

Karen Schettlinger   Wiebke Sieben

Technische Universität Dortmund

SFB 475: Reduction of Complexity in Multivariate Data Structures

technische universität dortmund

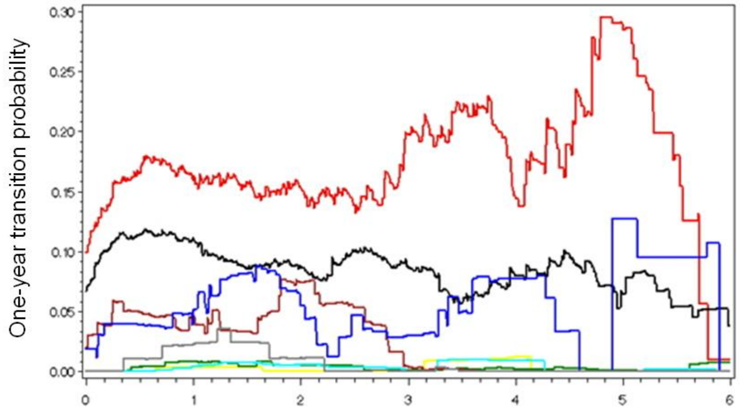
Collaborative Research Centre SFB 475
- Reduction of Complexity in Multivariate Data Structures -

Complex scientific problems in economics, engineering & life sciences

- Analysis of capital and labor markets
- Quality control in complex production processes
- Online monitoring in intensive care
- Causality of chronic diseases (cancer)

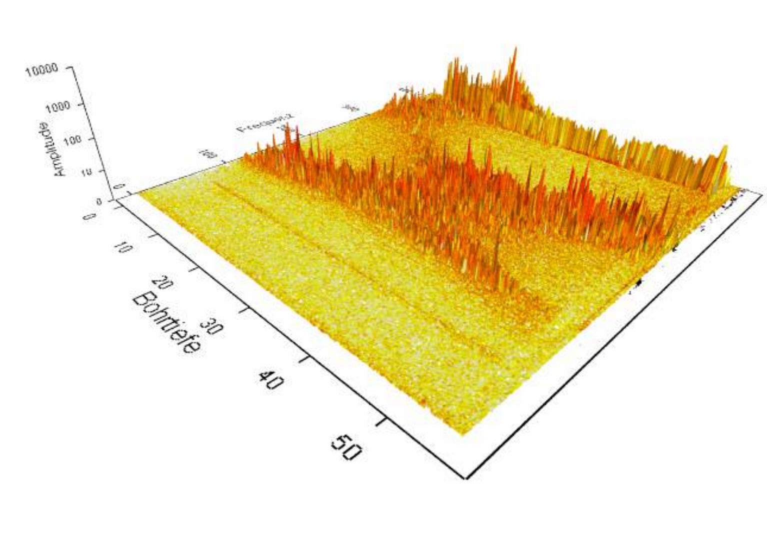
Complex Data Structures

High dynamics

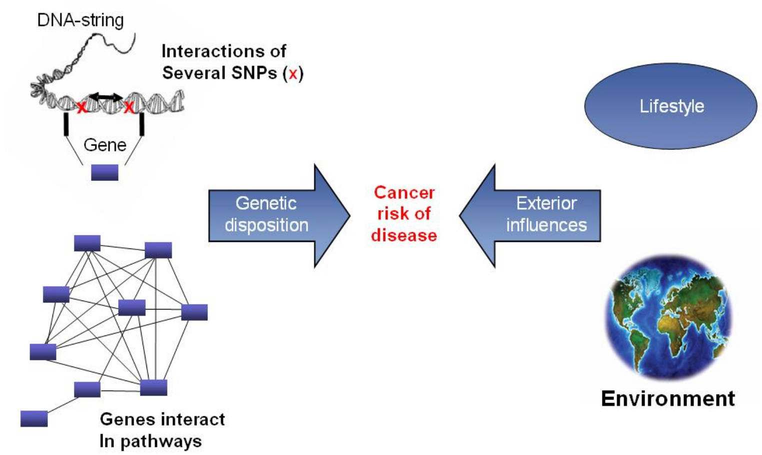


One-year migration rates for selected rating combinations over time

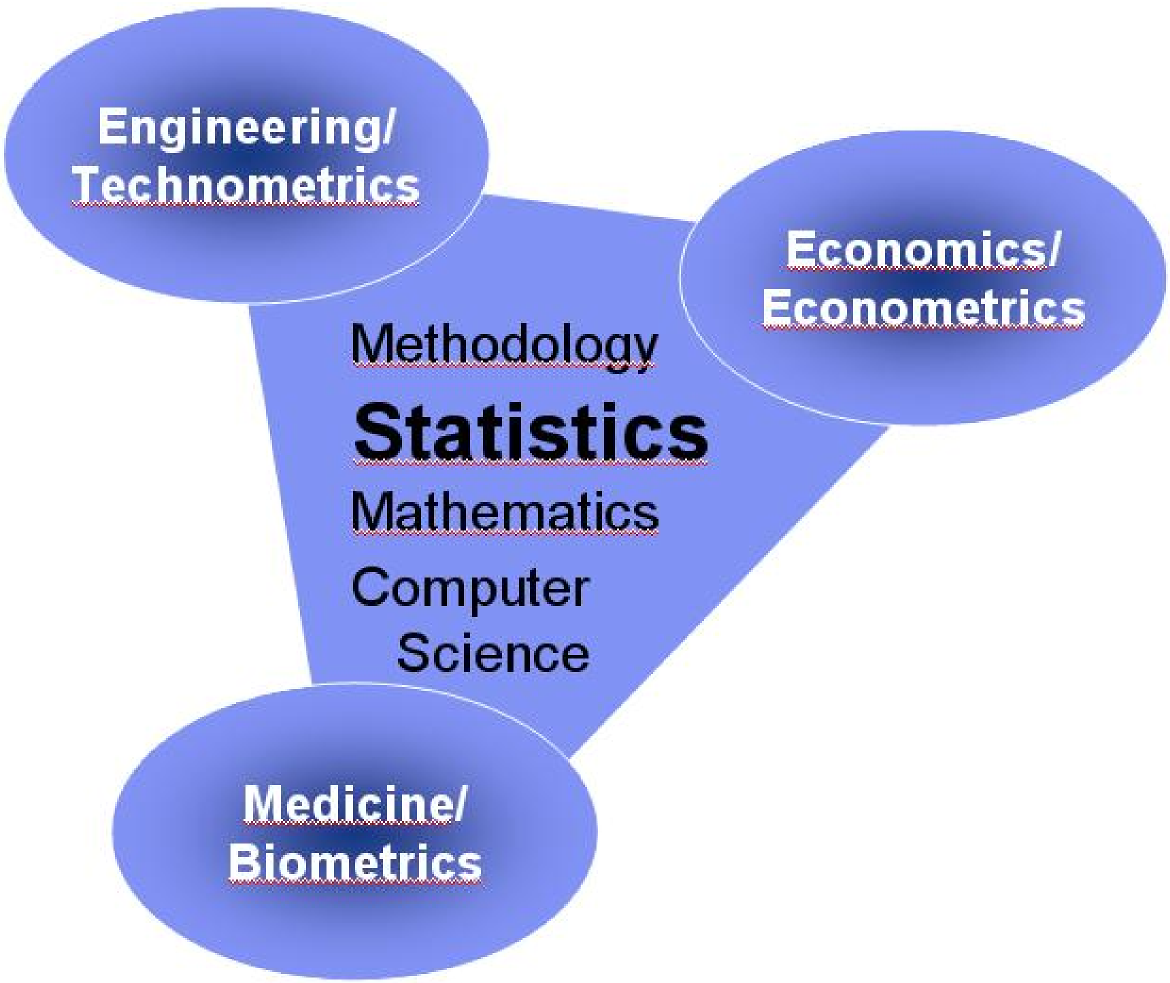
High dimensions



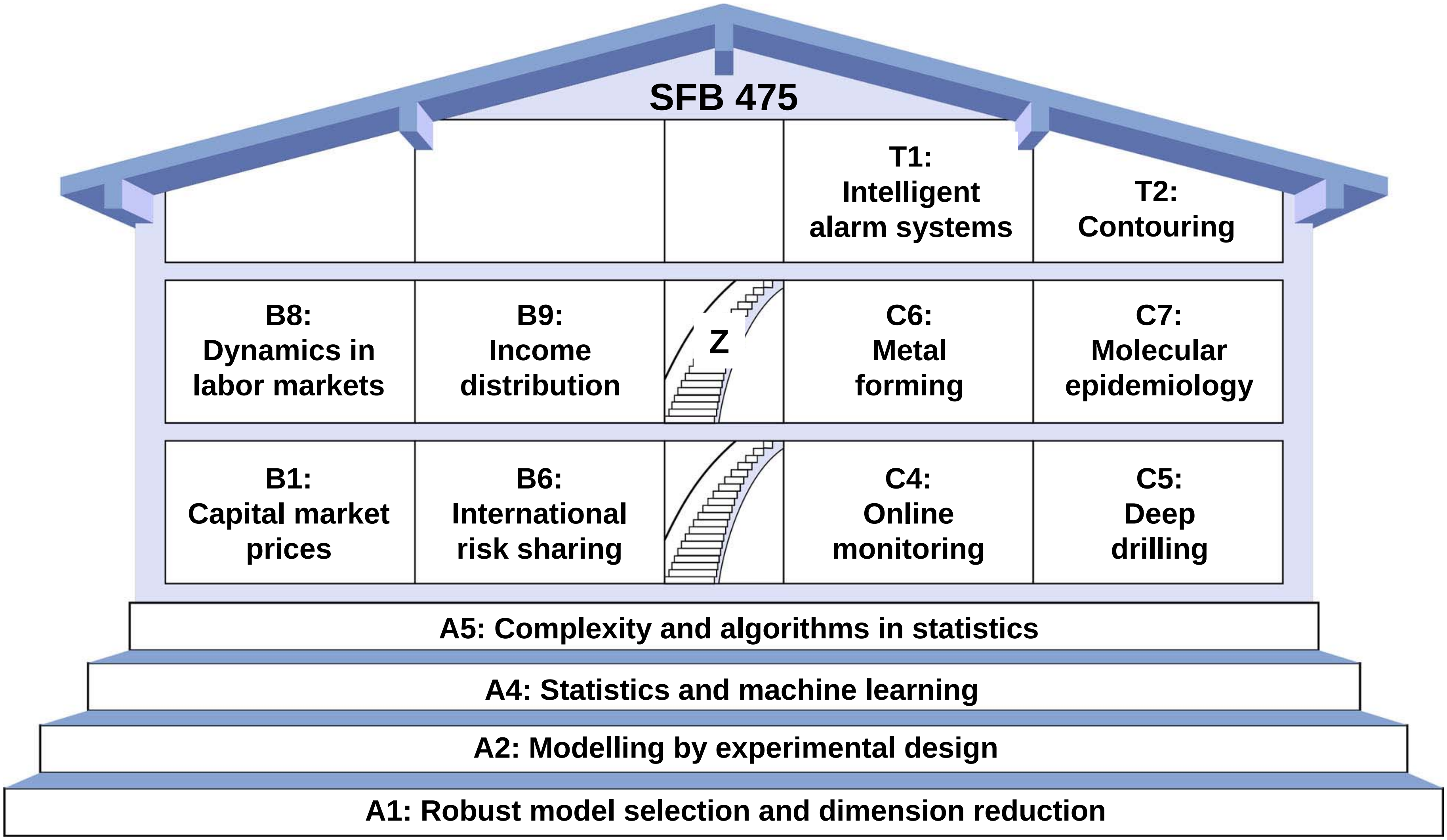
Complex dependence structures



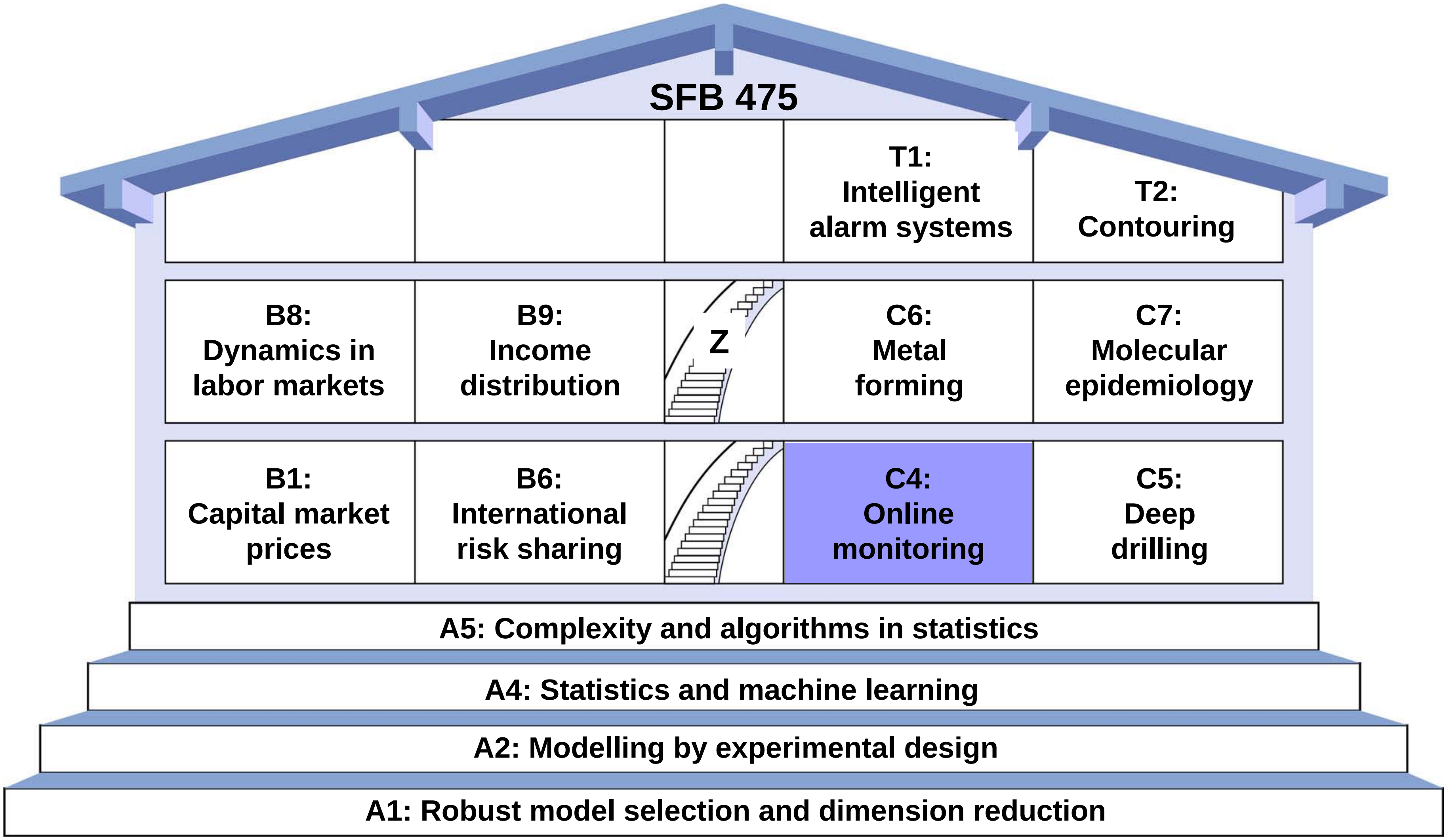
Collaborative Research Centre SFB 475
- Reduction of Complexity in Multivariate Data Structures -



Collaborative Research Centre SFB 475
- Reduction of Complexity in Multivariate Data Structures -

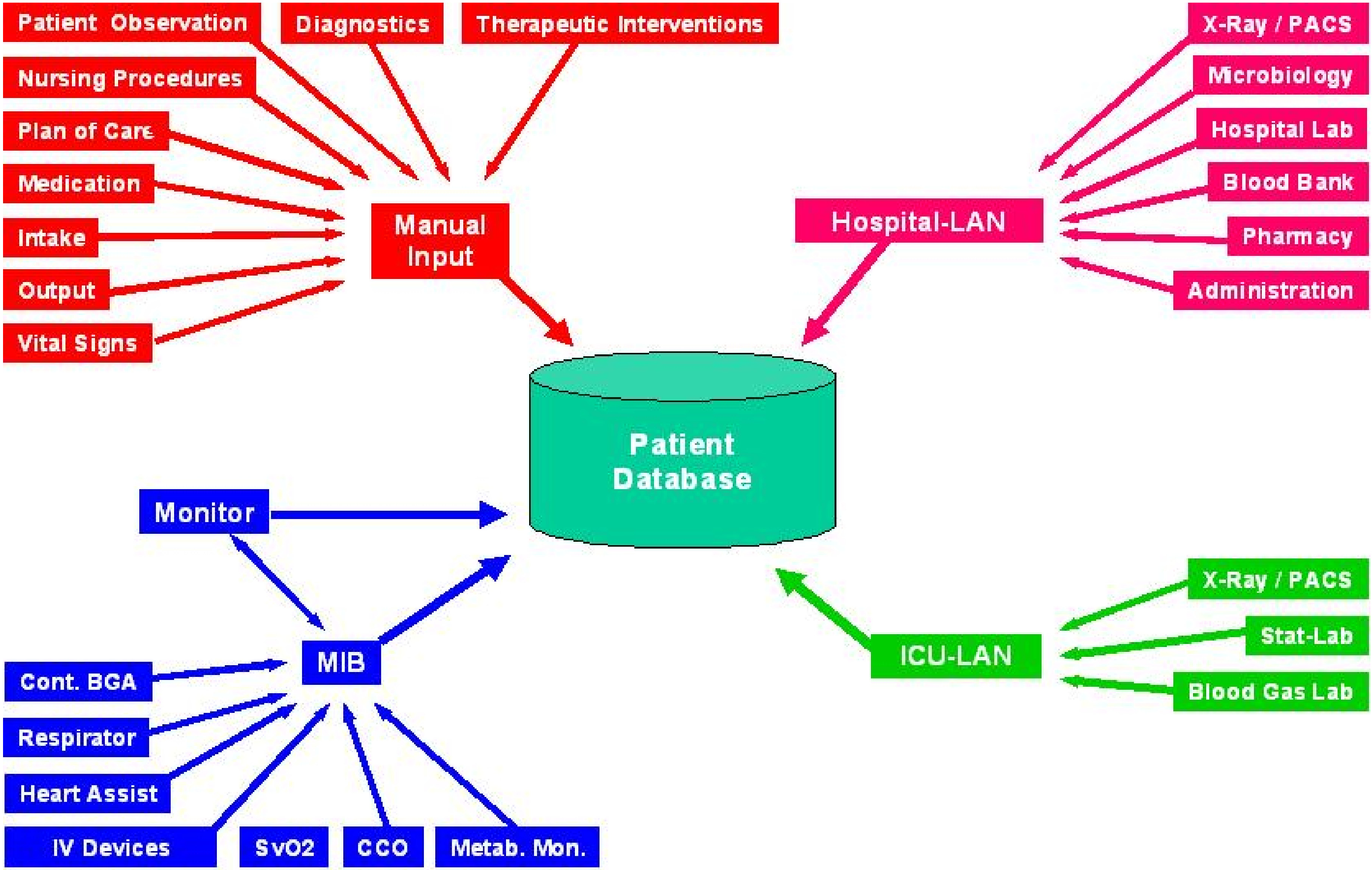


Collaborative Research Centre SFB 475
- Reduction of Complexity in Multivariate Data Structures -

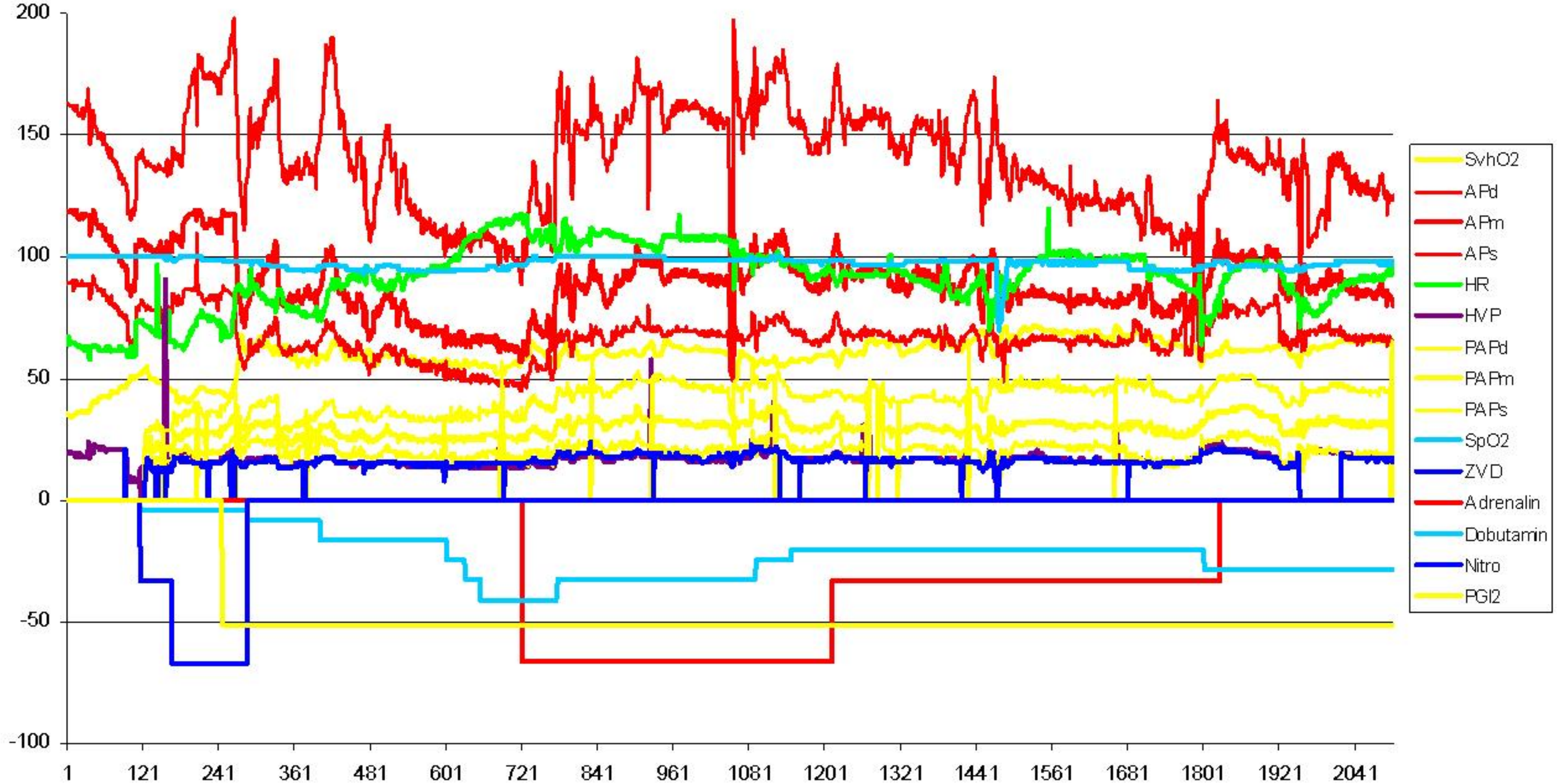


Intensive Care

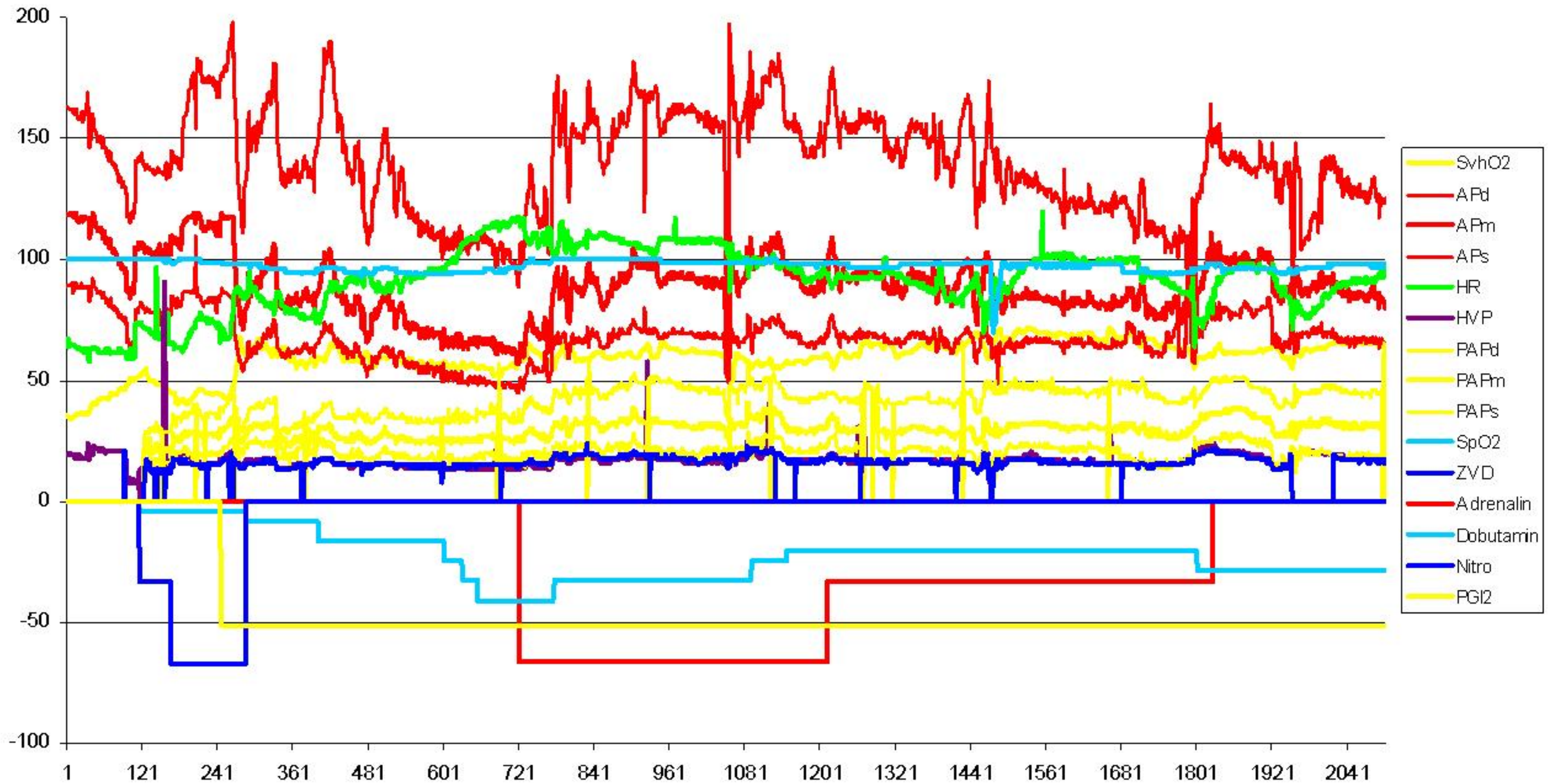
Data Acquisition



Motivation: Multivariate Time Series

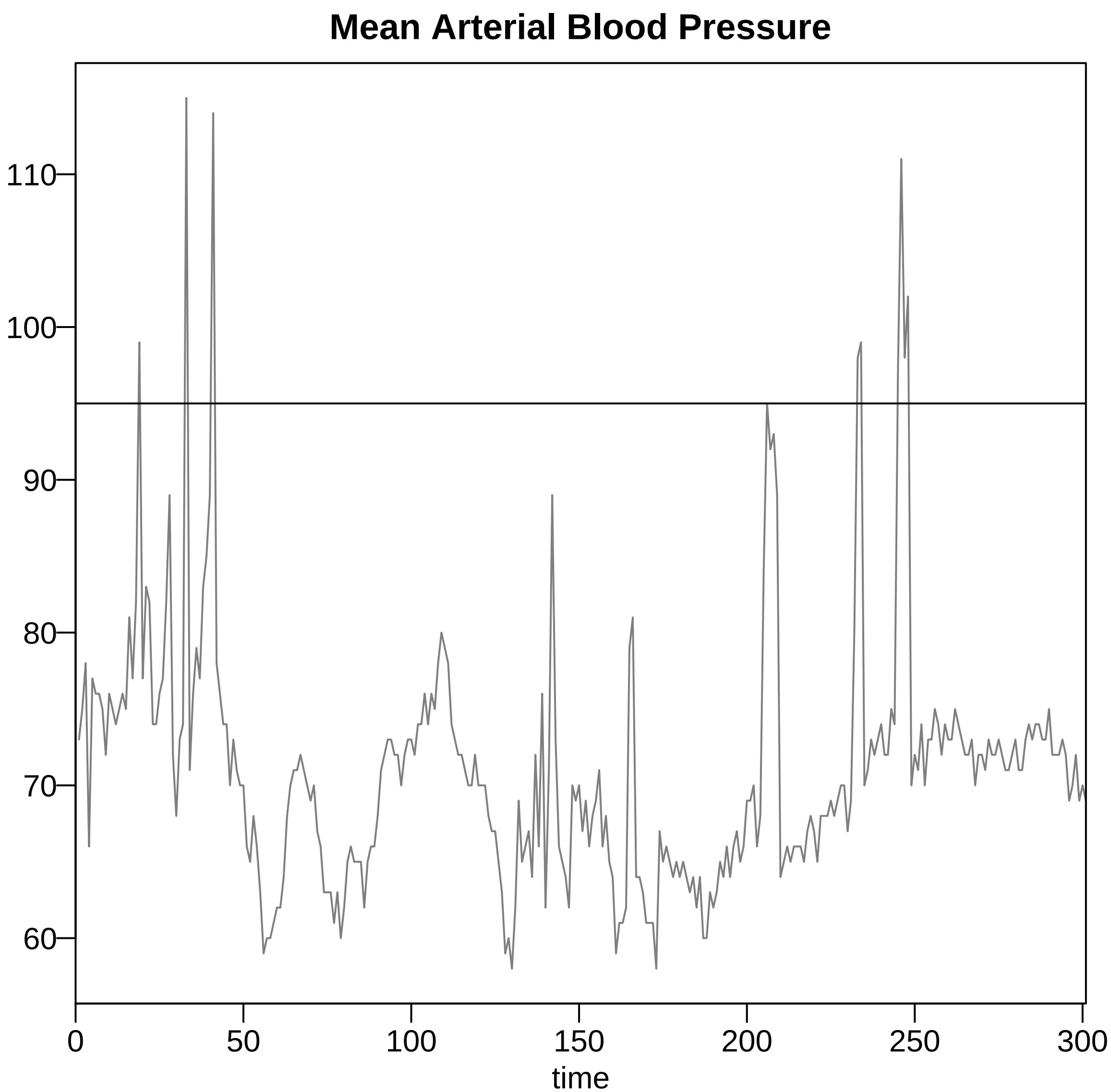


Motivation: Multivariate Time Series



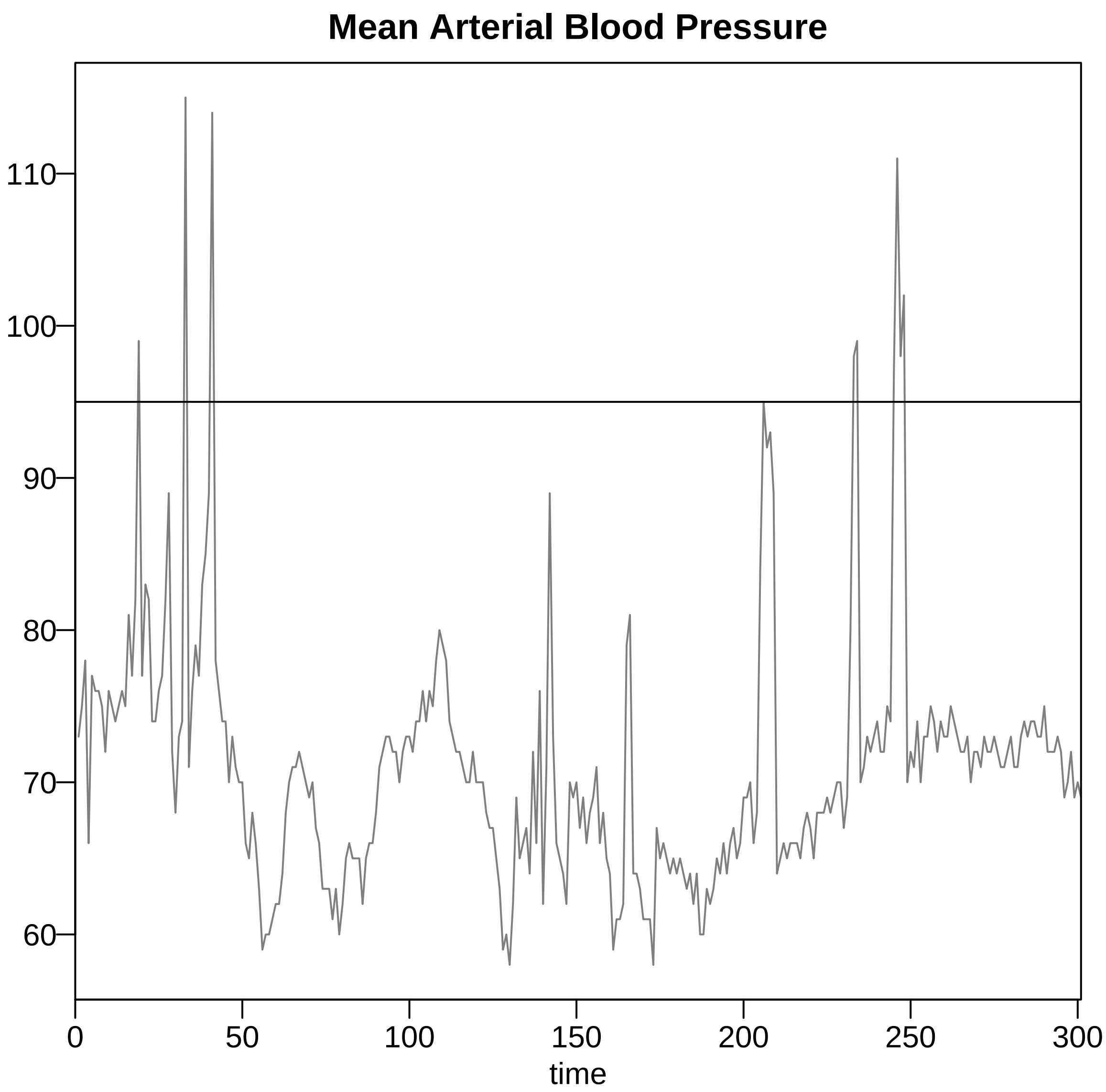
Objective: Online extraction of clinically relevant information from multivariate time series of the haemodynamic system

Motivation: Univariate Signal Extraction



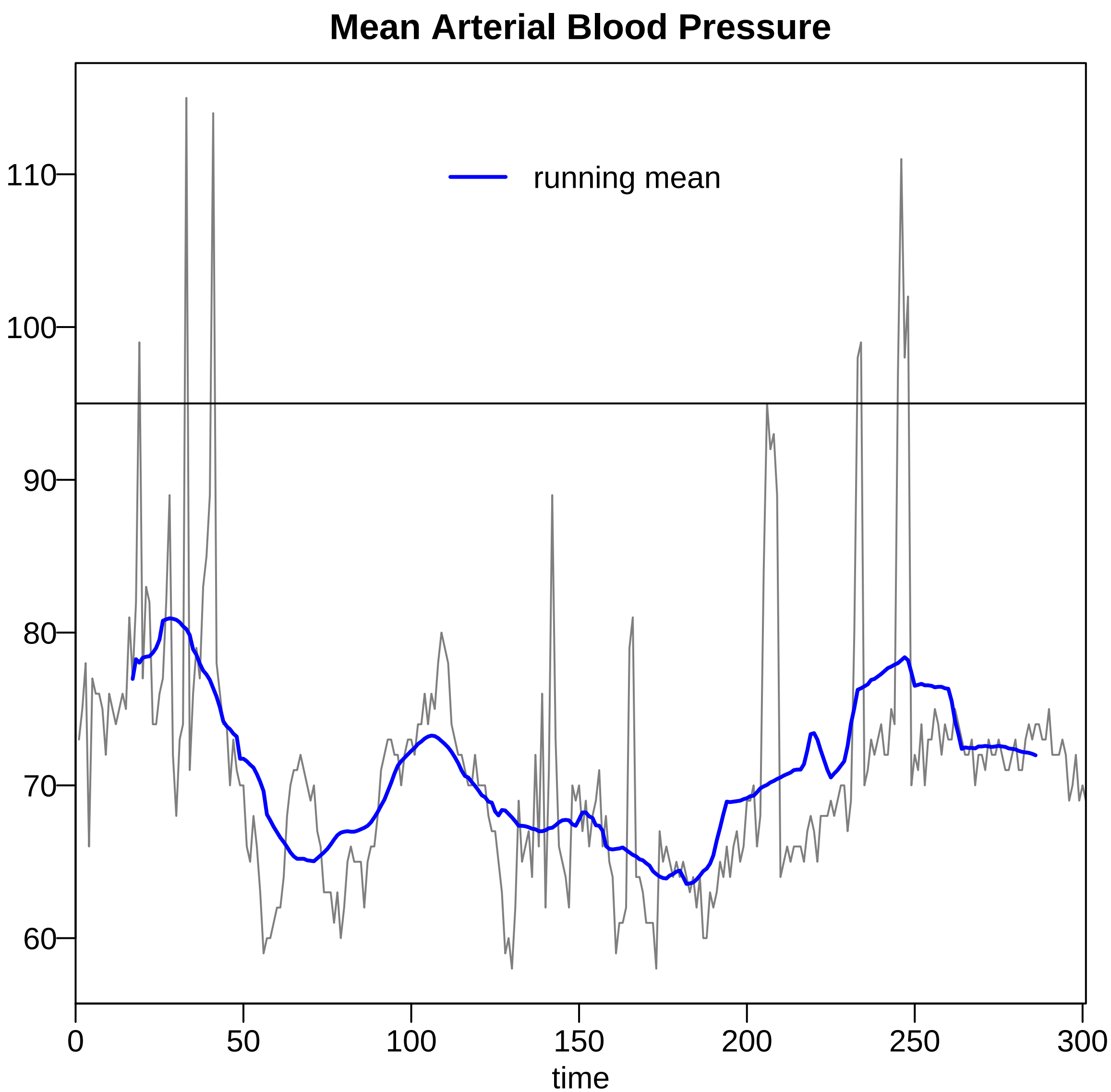
- Sudden changes and trends, no steady state
- Many artefacts
  $\Rightarrow$ False alarms

Motivation: Univariate Signal Extraction



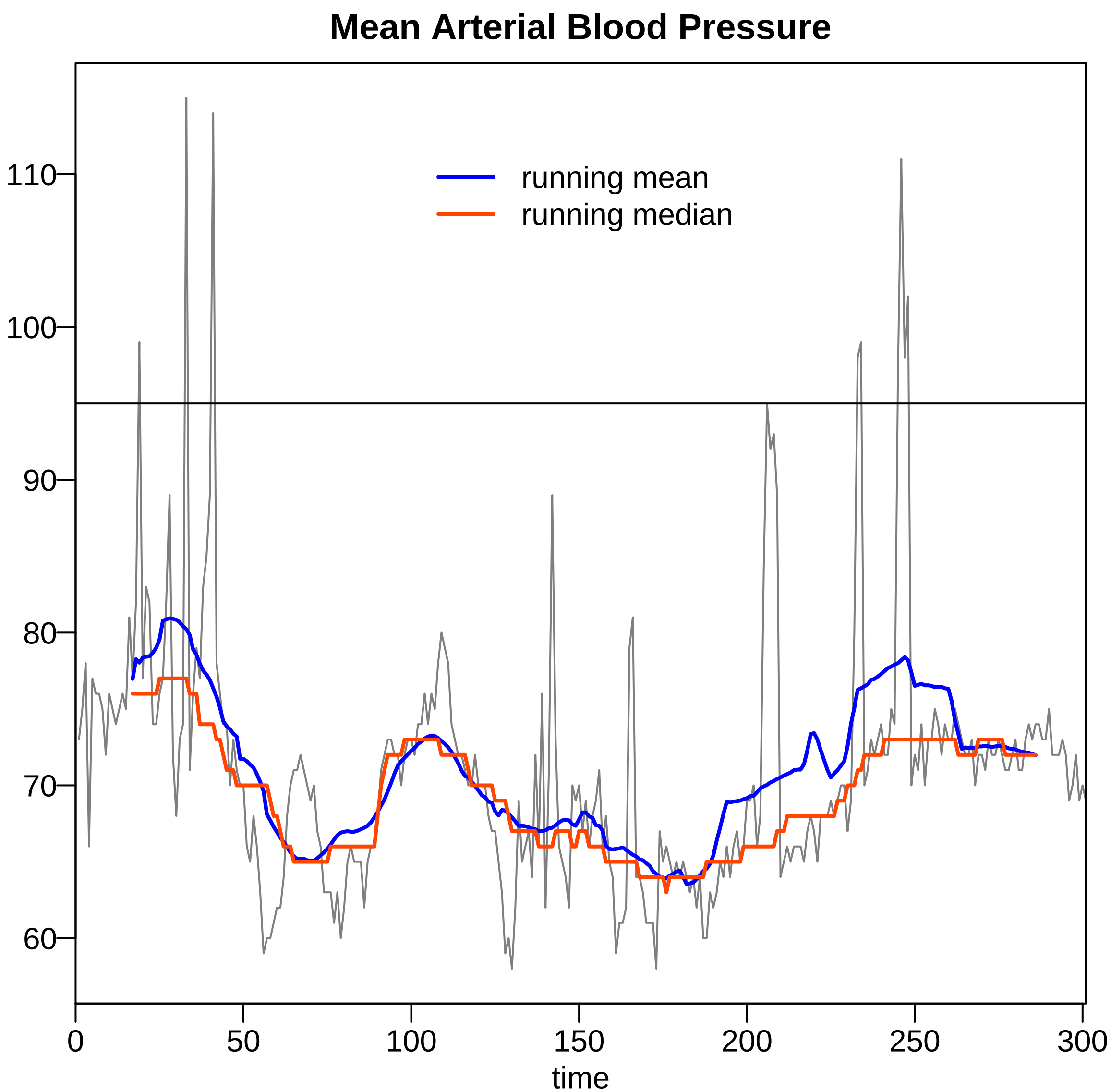
- Sudden changes and trends, no steady state
- Many artefacts
  $\Rightarrow$ False alarms
- New alarm system based on 'correct' signal extraction

Motivation: Univariate Signal Extraction



- Sudden changes and trends, no steady state
- Many artefacts
  $\Rightarrow$ False alarms
- New alarm system based on 'correct' signal extraction
- Location based filters:
  - Running mean not robust

Motivation: Univariate Signal Extraction



- Sudden changes and trends, no steady state
- Many artefacts
  $\Rightarrow$ False alarms
- New alarm system based on 'correct' signal extraction
- Location based filters:
  - Running mean not robust
  - Running median not smooth

Challenges

- Trends and level shifts in the signal
- Robustness against outliers
- Unknown dependence structures
- Short time delay
- Short computation time

Overview

I. Univariate signal extraction

- Methods
- Comparisons
- Applications

Overview

I. Univariate signal extraction

- Methods
- Comparisons
- Applications

II. Multivariate signal extraction

- Methods
- Applications

Overview

I. Univariate signal extraction

- Methods
- Comparisons
- Applications

II. Multivariate signal extraction

- Methods
- Applications

III. Alarm classification

I. Univariate Signal Extraction

Signal Extraction from Univariate Time Series

(Davies, Fried, Gather, 2004)

Model

$$x_t = \mu_t + \epsilon_t + \nu_t \ , \qquad t \in \mathbb{N}$$

Signal Extraction from Univariate Time Series

(Davies, Fried, Gather, 2004)

Model

$$x_t = \mu_t + \epsilon_t + \nu_t \; , \qquad t \in \mathbb{N}$$

Signal
smooth with a
few sudden shifts

Observational noise
symmetric
mean zero

Spiky noise
measurement
artefacts, ...

Signal Extraction from Univariate Time Series

(Davies, Fried, Gather, 2004)

Model

$$x_t = \mu_t + \epsilon_t + \nu_t \; , \qquad t \in \mathbb{N}$$

Signal
smooth with a
few sudden shifts

Observational noise
symmetric
mean zero

Spiky noise
measurement
artefacts, ...

Idea

Take moving windows $\{x_{t-m}, \ldots, x_t, \ldots, x_{t+m}\}$ to approximate μ_t

Model: Signal Extraction from Univariate Time Series

Local linear model within a time window of length $n = 2m + 1$:

$$x_{t+i} = \mu_t + \beta_t \, i + \varepsilon_{t,i}, \quad i = -m, \ldots, m$$

- **Estimation of the current level**
  either by $\hat{\mu}_t$ in centre or by $\hat{\mu}_{t+m}^{online} = \hat{\mu}_t + \hat{\beta}_t \, m$

Model: Signal Extraction from Univariate Time Series

Local linear model within a time window of length $n = 2m + 1$:

$$x_{t+i} = \mu_t + \beta_t \, i + \varepsilon_{t,i}, \quad i = -m, \ldots, m$$

- **Estimation of the current level**
  either by $\hat{\mu}_t$ in centre or by $\hat{\mu}_{t+m}^{online} = \hat{\mu}_t + \hat{\beta}_t \, m$

- **Choice of** m affects:

  - $\star$ Bias and variability $\Rightarrow$ Smoothness
  - $\star$ Robustness against outliers $\Rightarrow$ Stability
  - $\star$ Computation time $\Rightarrow$ Speed

Model: Signal Extraction from Univariate Time Series

Local linear model within a time window of length $n = 2m + 1$:

$$x_{t+i} = \mu_t + \beta_t\, i + \varepsilon_{t,i}, \quad i = -m, \ldots, m$$

- **Estimation of the current level**
  either by $\hat{\mu}_t$ in centre or by $\hat{\mu}_{t+m}^{online} = \hat{\mu}_t + \hat{\beta}_t\, m$

- **Choice of m** affects:

  ⋆ Bias and variability $\Rightarrow$ Smoothness
  ⋆ Robustness against outliers $\Rightarrow$ Stability
  ⋆ Computation time $\Rightarrow$ Speed

Estimation of level μ_t and slope β_t by robust linear regression

Robust Regression Methods

Repeated Median (RM)

(Siegel, 1982)

$$\hat{\beta}_t^{\textbf{RM}} = \operatorname*{med}_{i=-m}^{m} \left\{ \operatorname*{med}_{j \neq i} \frac{y_i - y_j}{i - j} \right\}$$

$$\hat{\mu}_t^{\textbf{RM}} = \operatorname*{med}_{i=-m}^{m} \left\{ x_{t+i} - \hat{\beta}_t^{\textbf{RM}} i \right\}$$

Robust Regression Methods

Repeated Median (RM)

(Siegel, 1982)

$$\hat{\beta}_t^{\textsf{RM}} = \operatorname*{med}_{i=-m}^{m} \left\{ \operatorname*{med}_{j \neq i} \frac{y_i - y_j}{i - j} \right\}$$

$$\hat{\mu}_t^{\textsf{RM}} = \operatorname*{med}_{i=-m}^{m} \left\{ x_{t+i} - \hat{\beta}_t^{\textsf{RM}} i \right\}$$

Least Median of Squares (LMS)

(Hampel, 1975; Rousseeuw, 1984)

$$(\hat{\mu}_t^{\textsf{LMS}}, \hat{\beta}_t^{\textsf{LMS}})' = \operatorname*{arg\,min}_{\hat{\mu}_t, \hat{\beta}_t} \left\{ \operatorname*{med}_{i=-m}^{m} \{ r_{t+i}^2 \} \right\}$$

Robust Regression Methods

L_1-Regression

(Edgeworth, 1887)

$$(\hat{\mu}_t^{\mathsf{L}_1}, \hat{\beta}_t^{\mathsf{L}_1})' = \arg\min_{\hat{\mu}_t, \hat{\beta}_t} \sum_{i=-m}^{m} |r_{t+i}|$$

Robust Regression Methods

L_1−Regression

(Edgeworth, 1887)

$$(\hat{\mu}_t^{\mathsf{L}_1}, \hat{\beta}_t^{\mathsf{L}_1})' = \arg\min_{\hat{\mu}_t, \hat{\beta}_t} \sum_{i=-m}^{m} |r_{t+i}|$$

Least Trimmed Squares

(Rousseeuw, 1983)

$$(\hat{\mu}_t^{\mathsf{LTS}}, \hat{\beta}_t^{\mathsf{LTS}})' = \arg\min_{\hat{\mu}_t, \hat{\beta}_t} \sum_{k=1}^{\lfloor n/2 \rfloor + 1} (r_t^2)_{k:n}$$

Robust Regression Methods

L_1-Regression (Edgeworth, 1887)

$$(\hat{\mu}_t^{\mathsf{L}_1}, \hat{\beta}_t^{\mathsf{L}_1})' = \arg\min_{\hat{\mu}_t, \hat{\beta}_t} \sum_{i=-m}^{m} |r_{t+i}|$$

Least Trimmed Squares (Rousseeuw, 1983)

$$(\hat{\mu}_t^{\mathsf{LTS}}, \hat{\beta}_t^{\mathsf{LTS}})' = \arg\min_{\hat{\mu}_t, \hat{\beta}_t} \sum_{k=1}^{\lfloor n/2 \rfloor + 1} (r_t^2)_{k:n}$$

Deepest Regression (Rousseeuw and Hubert, 1999)

$$(\hat{\mu}_t^{\mathsf{DR}}, \hat{\beta}_t^{\mathsf{DR}}) = \arg\max_{\hat{\mu}_t, \hat{\beta}_t} \left\{ rdepth\Big((\hat{\mu}_t, \hat{\beta}_t), \mathbf{x}_t \Big) \right\}$$

Comparisons: Robustness

Smallest number $k^\star$ of contaminated observations
which can cause a spike of any size in the extracted signal

$$k^\star = \min\{k : \sup\{\| T(\boldsymbol{z}) - T(\boldsymbol{x}) \|, \boldsymbol{z} \in U_k(\boldsymbol{x})\} = \infty\}$$

with $U_k(\boldsymbol{x}) = \{\boldsymbol{z} = (z_1, \ldots, z_n) : \sharp\{i : z_i \neq x_{t+i}\} = k\}$

Comparisons: Robustness

Smallest number $k^\star$ of contaminated observations
which can cause a spike of any size in the extracted signal

$$k^\star = \min\{k : \sup\{\| T(\boldsymbol{z}) - T(\boldsymbol{x}) \|, \boldsymbol{z} \in U_k(\boldsymbol{x})\} = \infty\}$$

$k^\star$	$\mathbf{L}_2$	$\mathbf{L}_1$	**LMS**	**LTS**	**RM**	**DR**
$n = 21$	1	7	10	10	10	≥ 6
$n = 31$	1	10	15	15	15	≥ 10

Comparisons: Efficiency

(Gather, Schettlinger, Fried, 2006)

Finite sample efficiencies for the **online estimates** $\hat{\mu}_t^{online}$ relative to Least Squares:

		LMS	LTS	RM	DR
standard normal errors	$n = 21$	.23	.22	.71	.62
	$n = 31$	.21	.20	.70	.61
rescaled t_3 errors	$n = 21$	.58	.56	1.44	1.37
	$n = 31$	.58	.57	1.50	1.42
shifted lognormal errors	$n = 21$	.44	.43	1.00	.93
	$n = 31$	.35	.33	.85	.78

$\longrightarrow$ Similar results for **LMS** & **LTS** and **RM** & **DR**

$\longrightarrow$ **RM** best

Comparisons: Computation Times

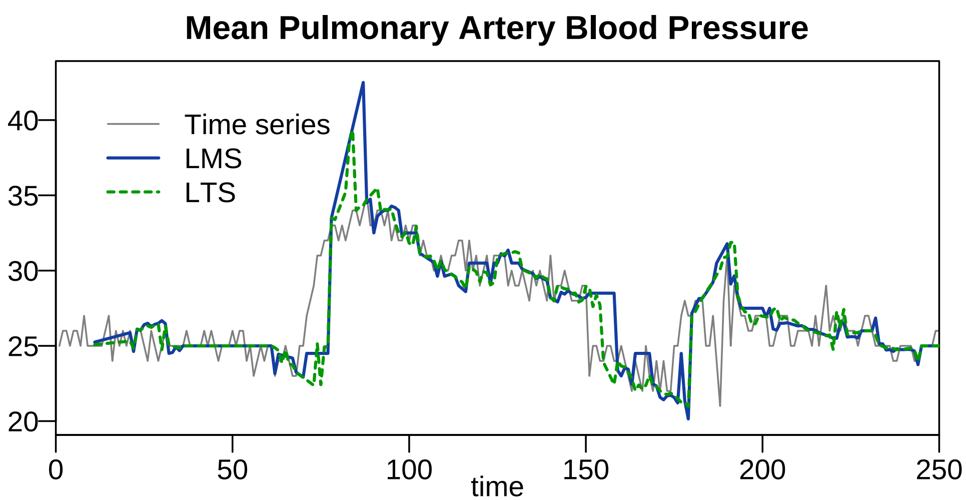
Simulated mean computation time of an update in milliseconds

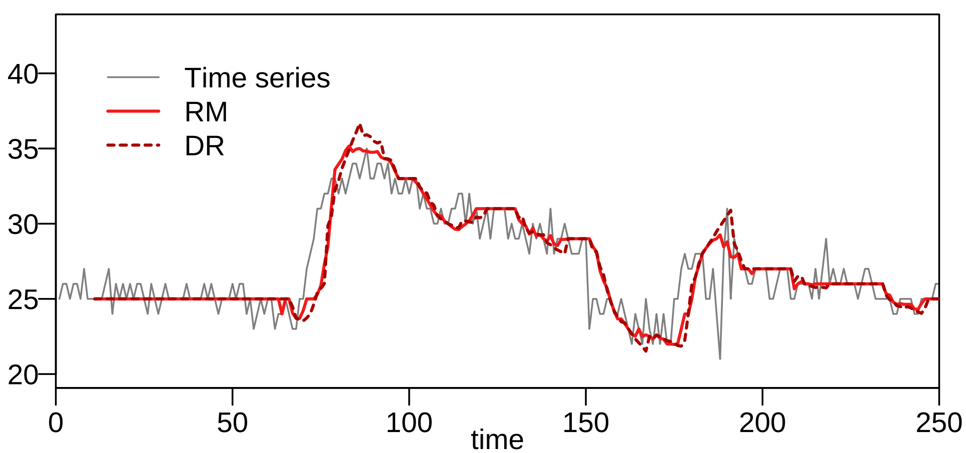
	LMS	LTS	RM	DR
$n = 21$	0.161	0.161	0.035	0.747
$n = 31$	0.323	0.324	0.049	0.956

Asymptotic computation time for an update

	LMS	LTS	RM	DR
Time	$O(n^2)$	$O(n^2)$	$O(n)$	$O(n \log^2 n)$
Memory space	$O(n^2)$	$O(n^2)$	$O(n^2)$	$O(n)$

Comparisons: Application to Real Data





Good performance of all methods in *constant* periods

Overestimation of the signal after the shift for **LMS**/**LTS**

RM/**DR** 'blur' shifts

LMS/**LTS** more affected by moderate data variation

RM/**DR** smoother

Summary

Robust regression works well for online signal extraction

- **LMS**/**LTS** preserve shifts but are unstable and perform poorly for trend changes
- **RM**/**DR** are stable and good at trend changes but smear shifts
- **RM** fastest, **DR** slowest method

Summary

Robust regression works well for online signal extraction

- **LMS**/**LTS** preserve shifts but are unstable and perform poorly for trend changes
- **RM**/**DR** are stable and good at trend changes but smear shifts
- **RM** fastest, **DR** slowest method

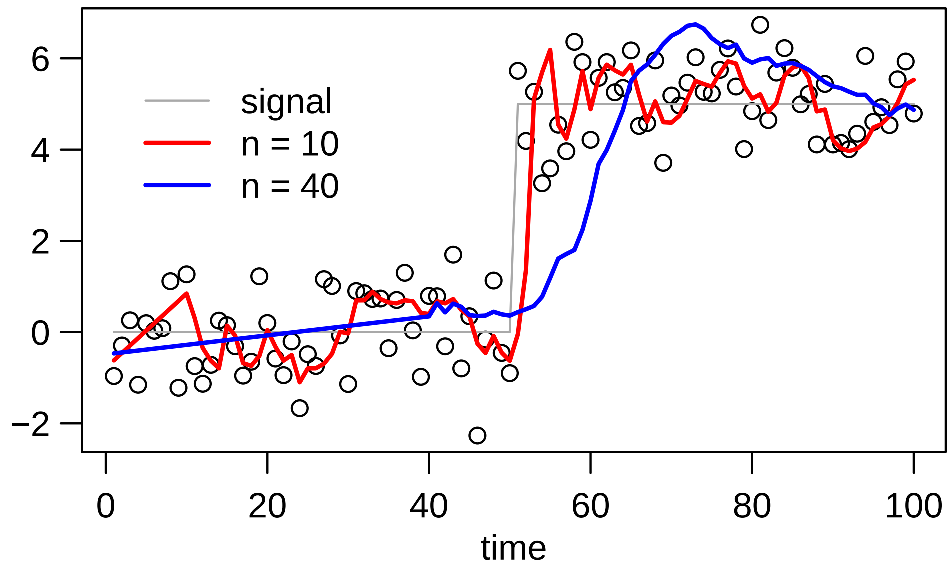
Overall best performance: **RM** regression

Improvements and Modifications

- Online outlier replacement and shift detection (Fried, 2004)
- Double window filters: (Bernholt, Fried, Gather, Wegener, 2006)
  Trimming based on robust estimate from (smaller) inner window;
  Final estimate from outer window
- Hybrid filters: (Fried, Bernholt, Gather, 2006)
  Combinations of subfilters applied to window halves
- Weighted repeated median filters (Fried, Einbeck, Gather, 2007)
- Adaptive window widths (Schettlinger, Fried, Gather, 2008)

➡ **R** package `robfilter` (Fried, Schettlinger, 2008)

Influence of the Window Width



n small

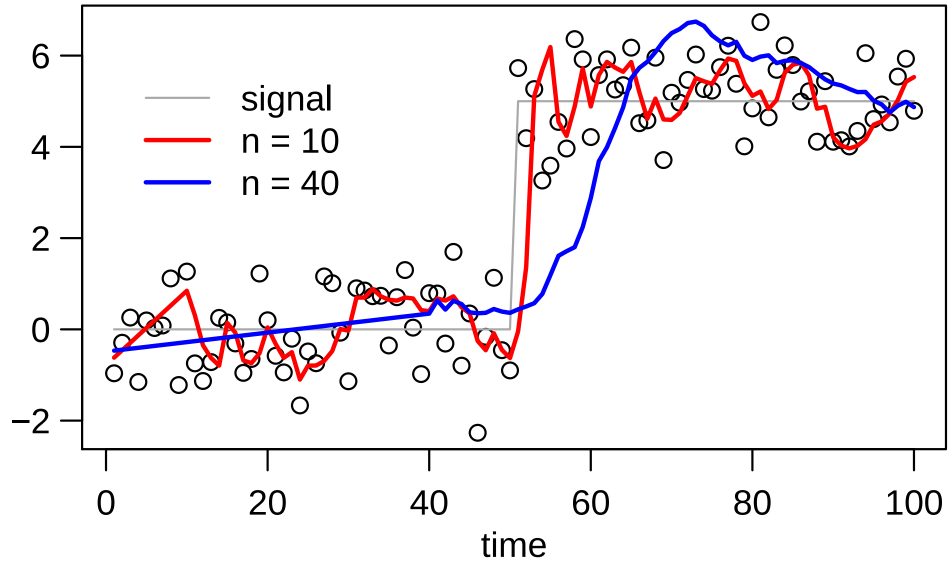
- small bias
- adapts quickly to changes
- short computation time

$\Leftrightarrow$

n large

- small variance
- smooth
- robust

Influence of the Window Width



n **small**

- small bias
- adapts quickly to changes
- short computation time

$\Leftrightarrow$

n **large**

- small variance
- smooth
- robust

➡ **Data adaptive choice of window width wanted**

Adaptive Choice of Window Width

(Schettlinger, Fried, Gather, 2008)

Idea

Use the 'balance' of the residual signs $\left(\sum_{i=1}^{n} \text{sign}(r_i) = 0 \right)$

RM approximation in current time window

Adaptive Choice of Window Width

(Schettlinger, Fried, Gather, 2008)

Idea

Use the 'balance' of the residual signs $\left(\sum_{i=1}^{n} \text{sign}(r_i) = 0 \right)$

RM approximation in current time window

$\downarrow$

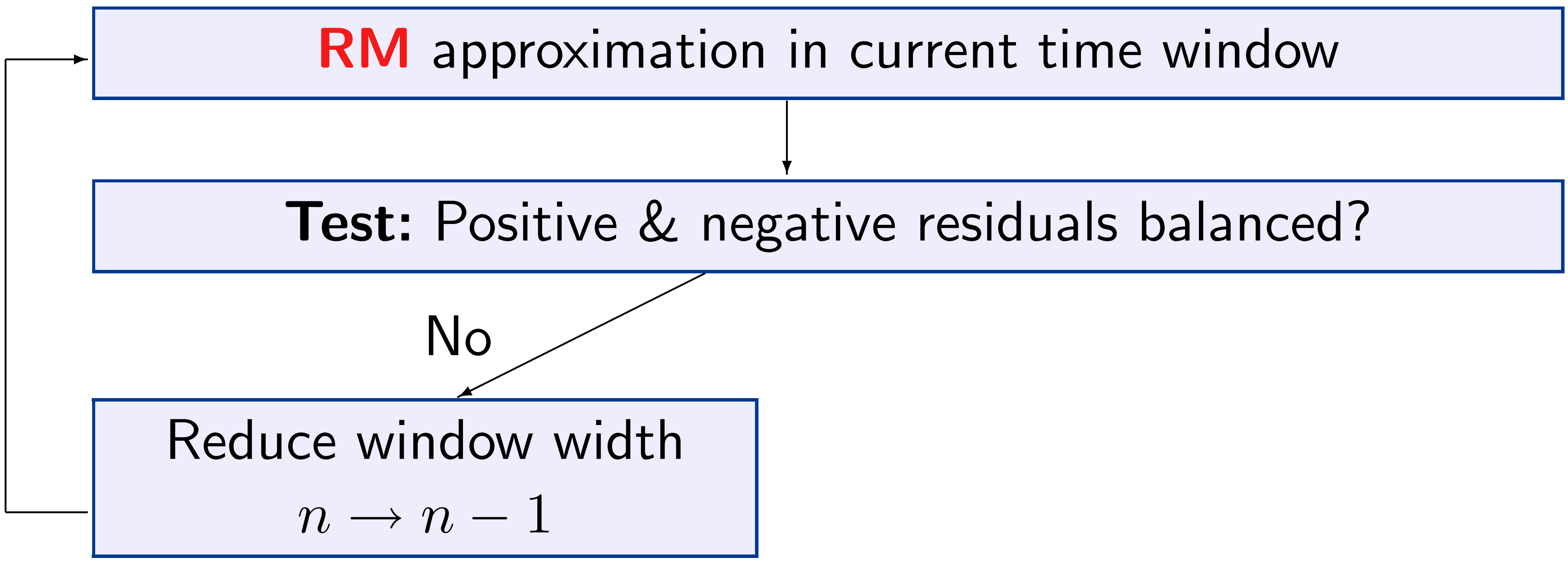
Test: Positive & negative residuals balanced?

Adaptive Choice of Window Width

(Schettlinger, Fried, Gather, 2008)

Idea

Use the 'balance' of the residual signs $\left(\sum_{i=1}^{n} \text{sign}(r_i) = 0 \right)$

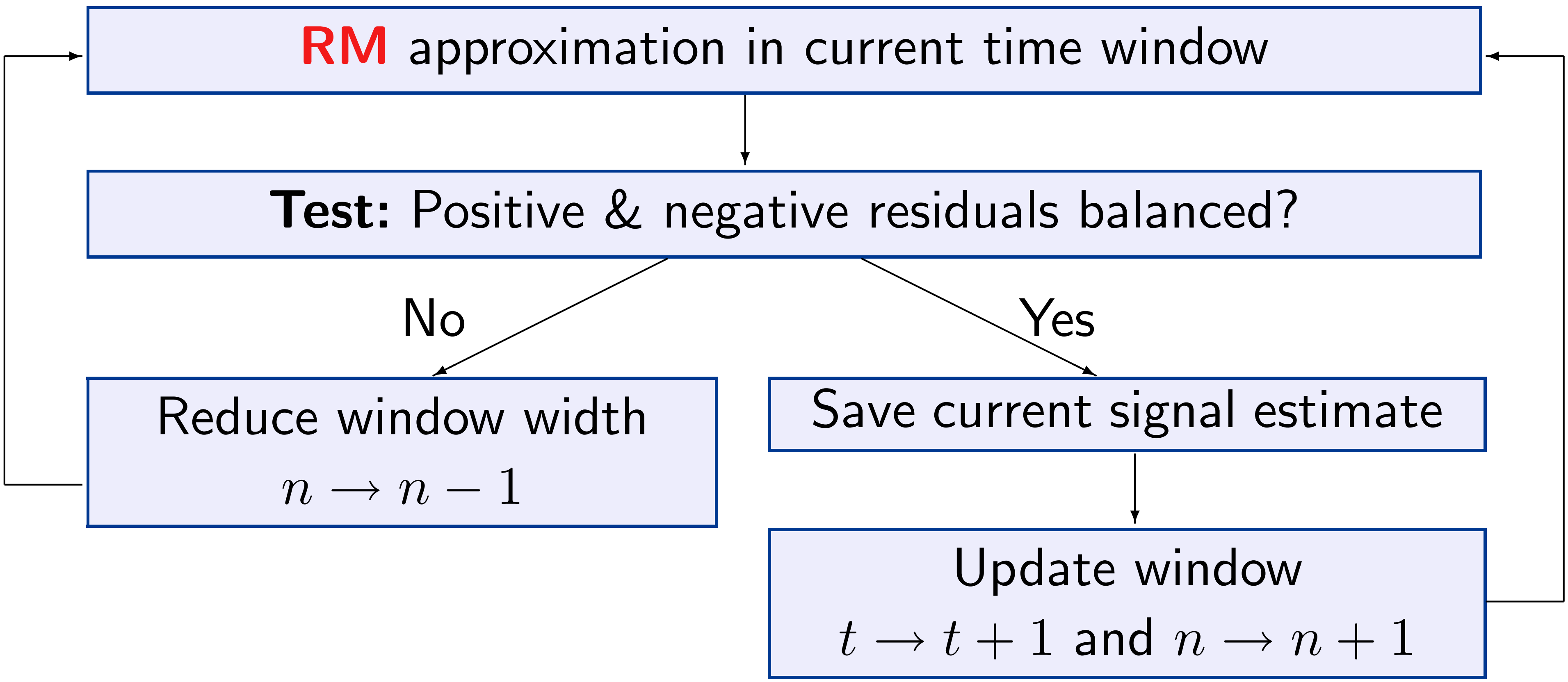


Adaptive Choice of Window Width

(Schettlinger, Fried, Gather, 2008)

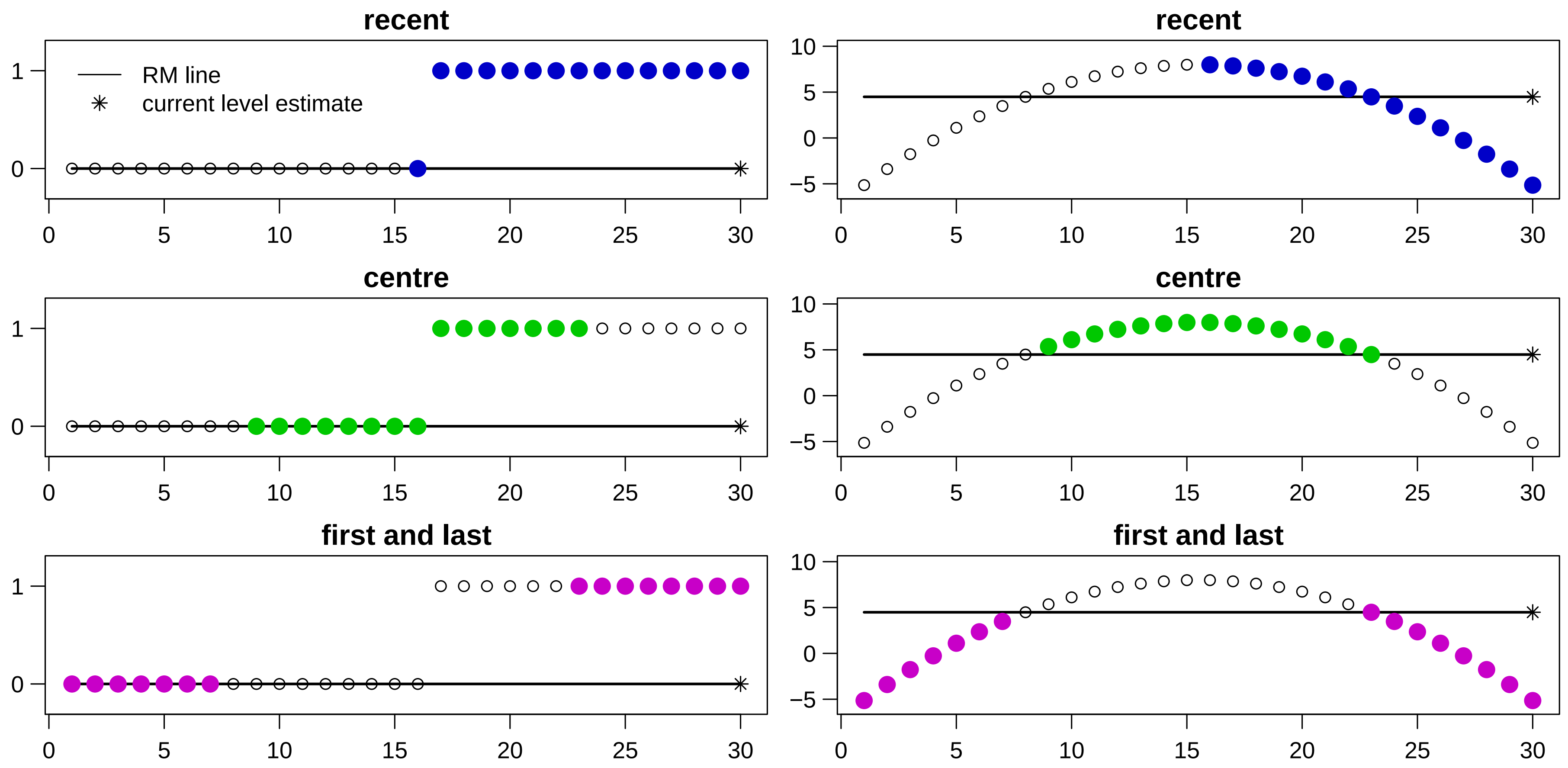
Idea

Use the 'balance' of the residual signs $\left(\sum_{i=1}^{n} \mathrm{sign}(r_i) = 0 \right)$



Selection of Residuals: Different Sets of Indices I

Example: $n = 30$ with $n_I = \lfloor n/2 \rfloor = 15$ selected time points



➡ **Appropriate selection by simulation**

Simulation Study

Aims

- Which index set I yields the 'best' results?
- How many values should I contain? $n_I = n/2$, $n/3$, $n/4$?
- Should n_I be independent of n? $n_I = 10$, 15, 30?

Simulation Study

Aims

- Which index set I yields the 'best' results?
- How many values should I contain? $n_I = n/2,\ n/3,\ n/4$?
- Should n_I be independent of n? $\quad n_I = 10,\ 15,\ 30$?

Results

Time delay in tracing a shift / trend change

- for I recent: small $n_I \longrightarrow$ small delay
- for I centre / first and last: large $n_I \longrightarrow$ small delay

Simulation Study

Aims

- Which index set I yields the 'best' results?
- How many values should I contain? $n_I = n/2,\ n/3,\ n/4$?
- Should n_I be independent of n? $\quad n_I = 10,\ 15,\ 30$?

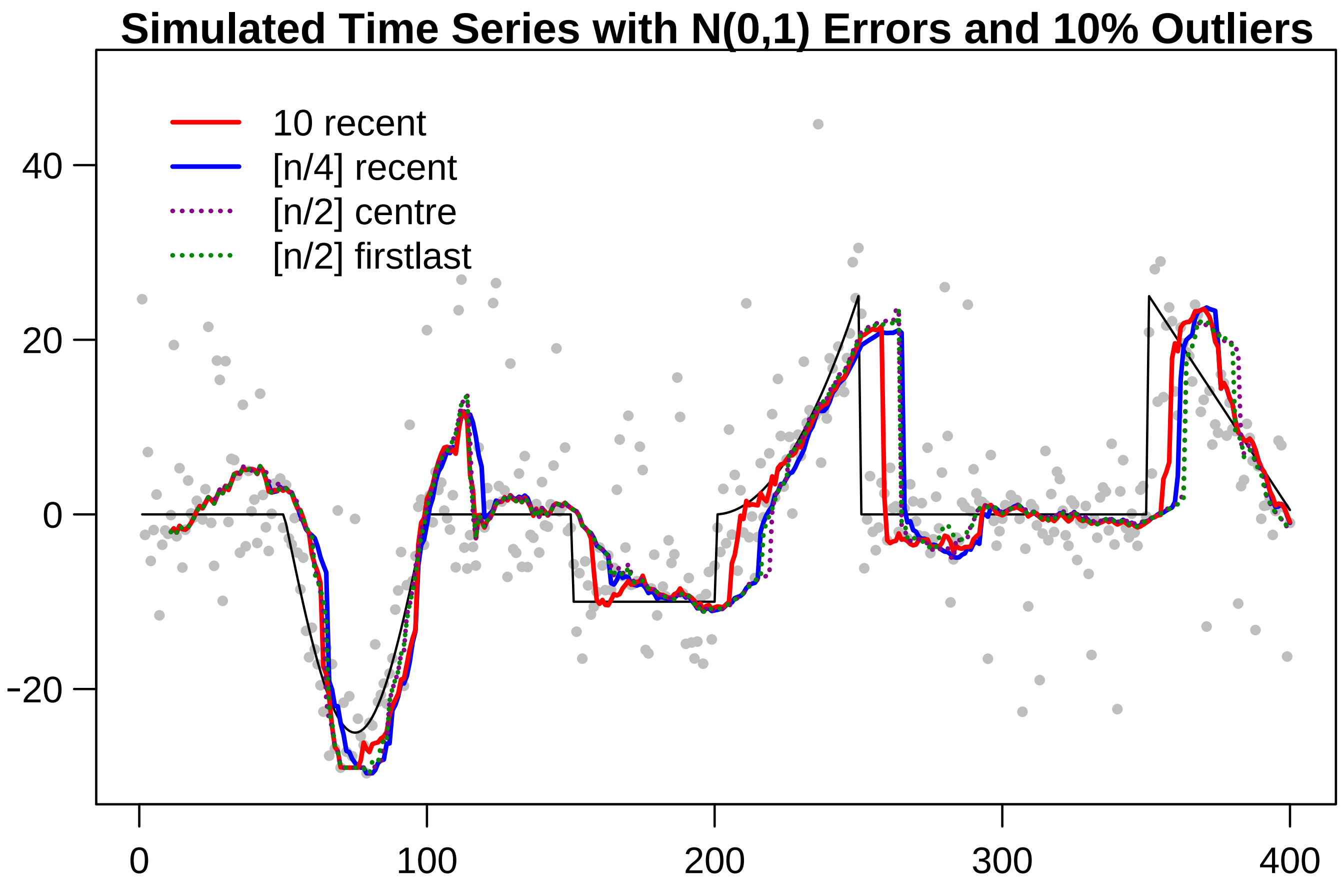
Results

Time delay in tracing a shift / trend change

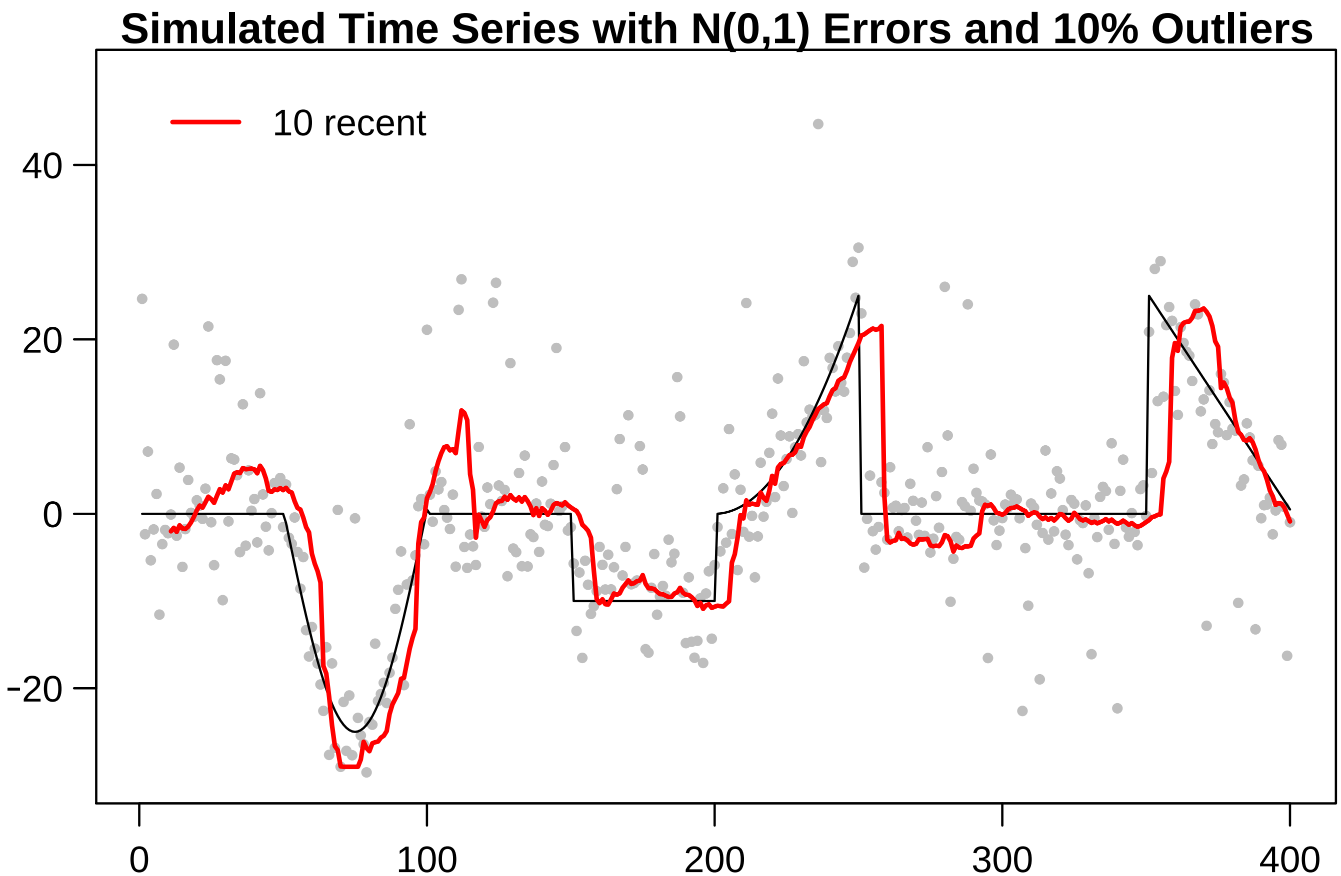
- for I recent: small $n_I \longrightarrow$ small delay
- for I centre / first and last: large $n_I \longrightarrow$ small delay

Best performance: I containing most recent time points

Application - Simulated Time Series



Application - Simulated Time Series



Best performance: I containing most recent time points
n_I small and independent of n

II. Multivariate Signal Extraction

Model: Signal Extraction for Multivariate Time Series

(Lanius, Gather, 2007)

Signal + noise model

$$\boldsymbol{x}(t) = \boldsymbol{\mu}(t) + \boldsymbol{\varepsilon}(t) + \boldsymbol{\nu}(t) \;, \qquad t \in \mathbb{N}$$

$\boldsymbol{\mu}(t) = (\mu_1(t), \ldots, \mu_k(t))^{\mathsf{T}}$ $k-$variate signal

$\boldsymbol{\varepsilon}(t) \in \mathbb{R}^k$ errors

$\boldsymbol{\nu}(t) \in \mathbb{R}^k$ outlier generating process

Model: Signal Extraction for Multivariate Time Series

(Lanius, Gather, 2007)

Signal + noise model

$$\boldsymbol{x}(t) = \boldsymbol{\mu}(t) + \boldsymbol{\varepsilon}(t) + \boldsymbol{\nu}(t) , \qquad t \in \mathbb{N}$$

$\boldsymbol{\mu}(t) = (\mu_1(t), \ldots, \mu_k(t))^{\mathsf{T}}$ $k-$variate signal

$\boldsymbol{\varepsilon}(t) \in \mathbb{R}^k$ errors

$\boldsymbol{\nu}(t) \in \mathbb{R}^k$ outlier generating process

Assumption: Each component $\mu_j(t)$, $j = 1, \ldots, k$, is locally linear

Idea

Approximate signal vector $\boldsymbol{\mu}(t)$
within each time window $\{\boldsymbol{x}(t-m), \ldots, \boldsymbol{x}(t), \ldots, \boldsymbol{x}(t+m)\}$
by k lines

Model: Signal Extraction for Multivariate Time Series

Local linear model within a time window of length $n = 2m + 1$:

$$\boxed{\boldsymbol{x}(t+i) = \boldsymbol{\mu}(t) + \boldsymbol{\beta}(t)\, i + \boldsymbol{\varepsilon}(t,i) + \boldsymbol{\eta}(t,i)\,, \quad i = -m, \ldots, m}$$

- Estimation of the current level by $\hat{\boldsymbol{\mu}}(t)$ in centre
- Use multivariate regression method which is
  - fast to compute
  - affine equivariant (ideally)
  - highly robust

Model: Signal Extraction for Multivariate Time Series

Local linear model within a time window of length $n = 2m + 1$:

$$\boldsymbol{x}(t+i) = \boldsymbol{\mu}(t) + \boldsymbol{\beta}(t)\, i + \boldsymbol{\varepsilon}(t,i) + \boldsymbol{\eta}(t,i)\,, \quad i = -m, \ldots, m$$

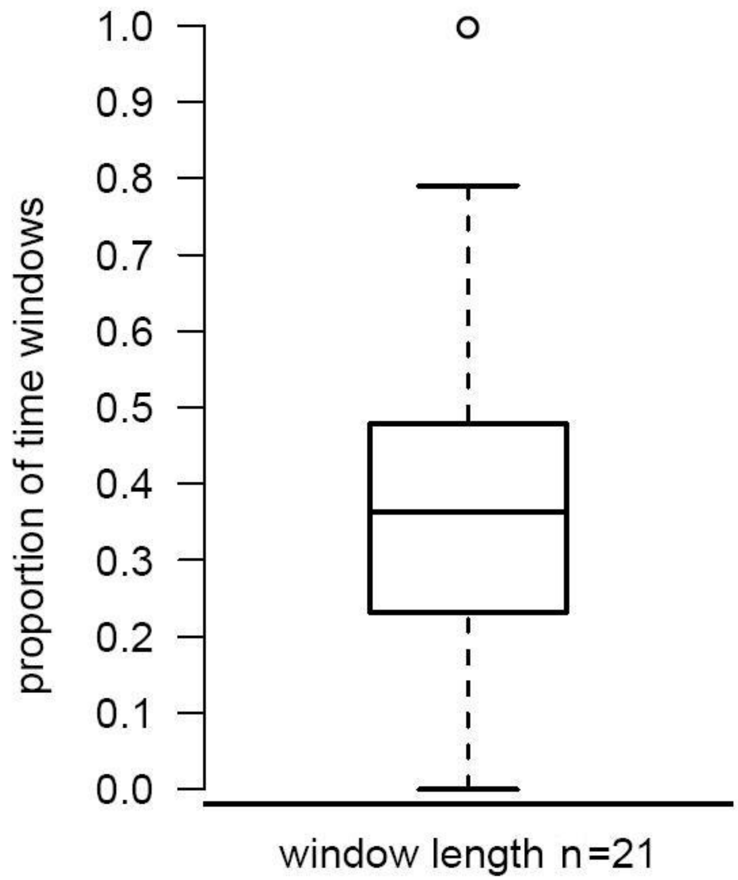
- Estimation of the current level by $\hat{\boldsymbol{\mu}}(t)$ in centre
- Use multivariate regression method which is
  - fast to compute
  - affine equivariant (ideally)
  - highly robust (breakdown point of approx. 50%).

  This affords the data to be in general position.

Data Situation

Haemodynamic variables measured on discrete scale

$\Rightarrow$ Observations not in general position:



On average the estimated MCD covariance matrix **implodes in 30-40%** of all time windows

Comparisons: Multivariate Regression Techniques

Local linear model for each t, $t = m + 1, \ldots, T - m$:

$$\boldsymbol{x}(t+i) = \boldsymbol{\mu}(t) + \boldsymbol{\beta}(t)\, i + \boldsymbol{\varepsilon}(t,i) + \boldsymbol{\eta}(t,i)\,, \quad i = -m, \ldots, m$$

Regression Method	Affine Equivariance	Optimal Breakdown Point	Computation
Least Squares	+	**0**	✓
Generalisation of	-		✓
robust univariate	-		✓
approaches	-		✓
MLTS Regression	+		approximative
MCD Regression	+		approximative

Comparisons: Multivariate Regression Techniques

Local linear model for each t, $t = m+1, \ldots, T-m$:

$$\boldsymbol{x}(t+i) = \boldsymbol{\mu}(t) + \boldsymbol{\beta}(t)\, i + \boldsymbol{\varepsilon}(t,i) + \boldsymbol{\eta}(t,i)\,, \quad i = -m, \ldots, m$$

Regression Method		Affine Equivariance	Optimal Breakdown Point	Computation
Least Squares		+	$\mathbf{0}$	✓
Generalisation of	L_1	-	$\sim 1/3$	✓
robust univariate	**LMS**	-	$\lfloor n/2 \rfloor / n$	✓
approaches	**RM**	-	$\lfloor n/2 \rfloor / n$	✓
MLTS Regression		+		approximative
MCD Regression		+		approximative

Comparisons: Multivariate Regression Techniques

Local linear model for each t, $t = m+1, \ldots, T-m$:

$$\boldsymbol{x}(t+i) = \boldsymbol{\mu}(t) + \boldsymbol{\beta}(t)\, i + \boldsymbol{\varepsilon}(t,i) + \boldsymbol{\eta}(t,i)\,, \quad i = -m, \ldots, m$$

Regression Method		Affine Equivariance	Optimal Breakdown Point	Computation
Least Squares		+	$\mathbf{0}$	✓
Generalisation of	**L**$_1$	-	$\sim 1/3$	✓
robust univariate	**LMS**	-	$\lfloor n/2 \rfloor / n$	✓
approaches	**RM**	-	$\lfloor n/2 \rfloor / n$	✓
MLTS Regression		+	$\lfloor (n-k)/2 \rfloor / n$	approximative
MCD Regression		+	$\lfloor (n-k)/2 \rfloor / n$	approximative

Procedure for Multivariate Signal Extraction

(Lanius, Gather, 2007)

Within each time window $\{\boldsymbol{x}(t+i),\, i=-m,\ldots,m\}$:

1. Use univariate **RM** to find $\hat{\mu}_j(t)$ and $\hat{\beta}_j(t)$ for each j

Procedure for Multivariate Signal Extraction

(Lanius, Gather, 2007)

Within each time window $\{\boldsymbol{x}(t+i),\, i = -m, \ldots, m\}$:

1. Use univariate **RM** to find $\hat{\mu}_j(t)$ and $\hat{\beta}_j(t)$ for each j

2. Find residuals $\boldsymbol{r}(t+i) = \boldsymbol{x}(t+i) - \hat{\boldsymbol{\mu}}(t) - i\hat{\boldsymbol{\beta}}(t)$

Procedure for Multivariate Signal Extraction

(Lanius, Gather, 2007)

Within each time window $\{\boldsymbol{x}(t+i),\, i=-m,\ldots,m\}$:

1. Use univariate **RM** to find $\hat{\mu}_j(t)$ and $\hat{\beta}_j(t)$ for each j
2. Find residuals $\boldsymbol{r}(t+i) = \boldsymbol{x}(t+i) - \hat{\boldsymbol{\mu}}(t) - i\hat{\boldsymbol{\beta}}(t)$
3. Use modified orthogonalized Gnanadesikan-Kettenring estimator

Procedure for Multivariate Signal Extraction

(Lanius, Gather, 2007)

Within each time window $\{\boldsymbol{x}(t+i),\, i=-m,\ldots,m\}$:

1. Use univariate **RM** to find $\hat{\mu}_j(t)$ and $\hat{\beta}_j(t)$ for each j

2. Find residuals $\boldsymbol{r}(t+i) = \boldsymbol{x}(t+i) - \hat{\boldsymbol{\mu}}(t) - i\hat{\boldsymbol{\beta}}(t)$

3. Use modified OGK_{Q_n}-estimator as robust estimate of the local covariance matrix $\boldsymbol{\Sigma}(t)$ of $\boldsymbol{r}(t+i)$

Procedure for Multivariate Signal Extraction

(Lanius, Gather, 2007)

Within each time window $\{\boldsymbol{x}(t+i),\, i=-m,\dots,m\}$:

1. Use univariate **RM** to find $\hat{\mu}_j(t)$ and $\hat{\beta}_j(t)$ for each j
2. Find residuals $\boldsymbol{r}(t+i) = \boldsymbol{x}(t+i) - \hat{\boldsymbol{\mu}}(t) - i\hat{\boldsymbol{\beta}}(t)$
3. Use modified OGK$_{Q_n}$-estimator as robust estimate of the local covariance matrix $\boldsymbol{\Sigma}(t)$ of $\boldsymbol{r}(t+i)$
4. Find $I_t = \{i = -m, \dots, m : \boldsymbol{r}(t+i)^{\mathsf{T}} \hat{\boldsymbol{\Sigma}}(t)^{-1} \boldsymbol{r}(t+i) \le d_n\}$

Procedure for Multivariate Signal Extraction

(Lanius, Gather, 2007)

Within each time window $\{\boldsymbol{x}(t+i),\, i=-m,\ldots,m\}$:

1. Use univariate **RM** to find $\hat{\mu}_j(t)$ and $\hat{\beta}_j(t)$ for each j
2. Find residuals $\boldsymbol{r}(t+i) = \boldsymbol{x}(t+i) - \hat{\boldsymbol{\mu}}(t) - i\hat{\boldsymbol{\beta}}(t)$
3. Use modified OGK$_{Q_n}$-estimator as robust estimate of the local covariance matrix $\boldsymbol{\Sigma}(t)$ of $\boldsymbol{r}(t+i)$
4. Find $I_t = \{i = -m,\ldots,m :\ \boldsymbol{r}(t+i)^{\mathsf{T}}\hat{\boldsymbol{\Sigma}}(t)^{-1}\boldsymbol{r}(t+i) \le d_n\}$
5. Calculate $\hat{\boldsymbol{\beta}}^{\text{new}}(t)$ and $\hat{\boldsymbol{\mu}}^{\text{new}}(t)$ by Least Squares Regression based on $\{(t+i, \boldsymbol{x}(t+i)), i \in I_t\}$

Properties

- Very robust procedure (optimal breakdown point of 50%)
- Procedure is not affine equivariant, but:
  with correlated errors more efficient than univariate methods
  and affine equivariant methods with similar breakdown point
- Fast computation
- Applicable to discrete data

Also: Online version with adaptive window width!

Adaptive Multivariate Online Signal Extraction

(Borowski, Schettlinger, Gather, 2008)

Within each time window $\{\boldsymbol{x}(t+i), \boldsymbol{i = -n(t-1), \ldots, 0}\}$:

1. **Use adaptive univariate RM** to find $\hat{\mu}_j(t)$ and $\hat{\beta}_j(t)$ for each j and **determine new window width $\boldsymbol{n(t)}$**

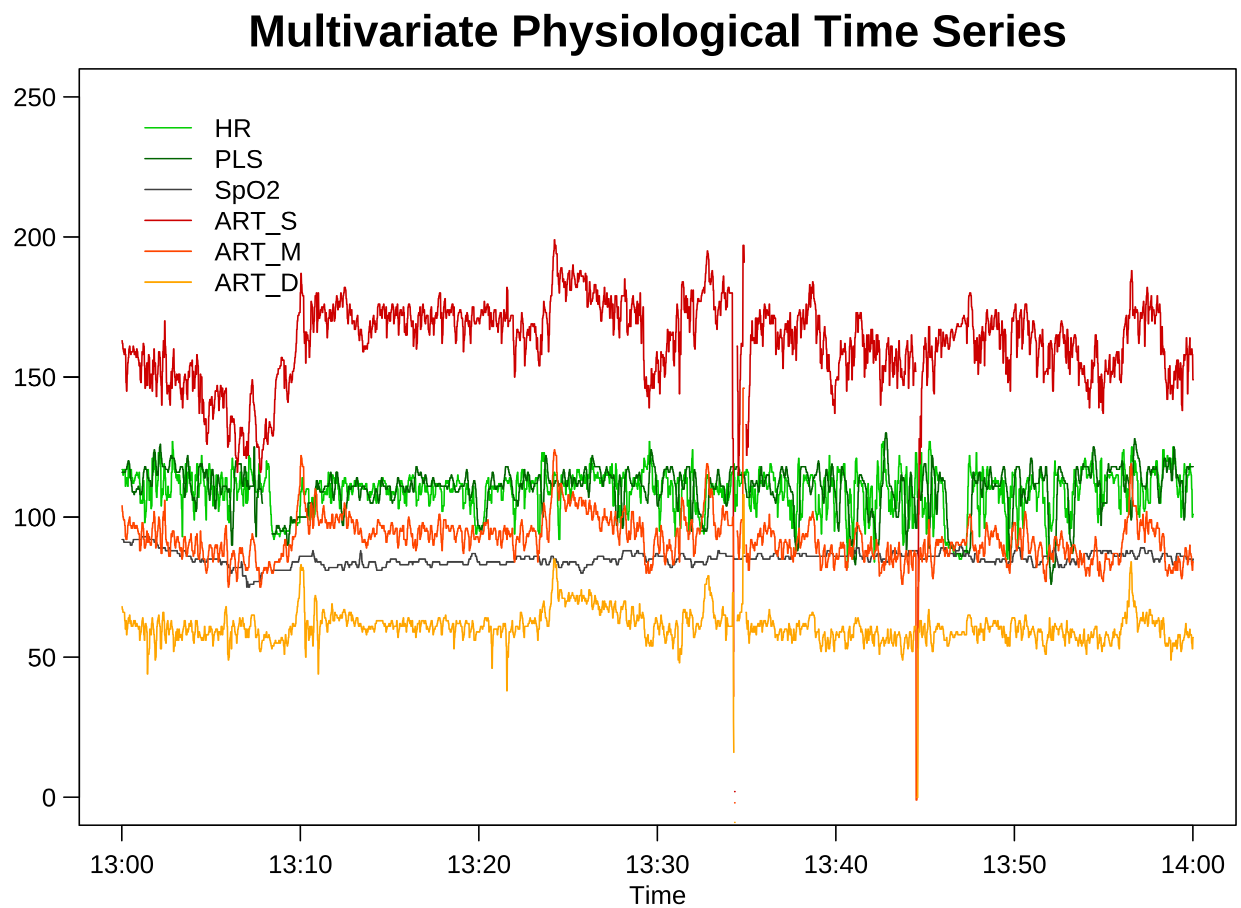
2. Find residuals $\boldsymbol{r}(t+i) = \boldsymbol{x}(t+i) - \hat{\boldsymbol{\mu}}(t) - i\hat{\boldsymbol{\beta}}(t)$

3. Use modified OGK_{Q_n}-estimator as robust estimate of the local covariance matrix $\boldsymbol{\Sigma}(t)$ of $\boldsymbol{r}(t+i)$

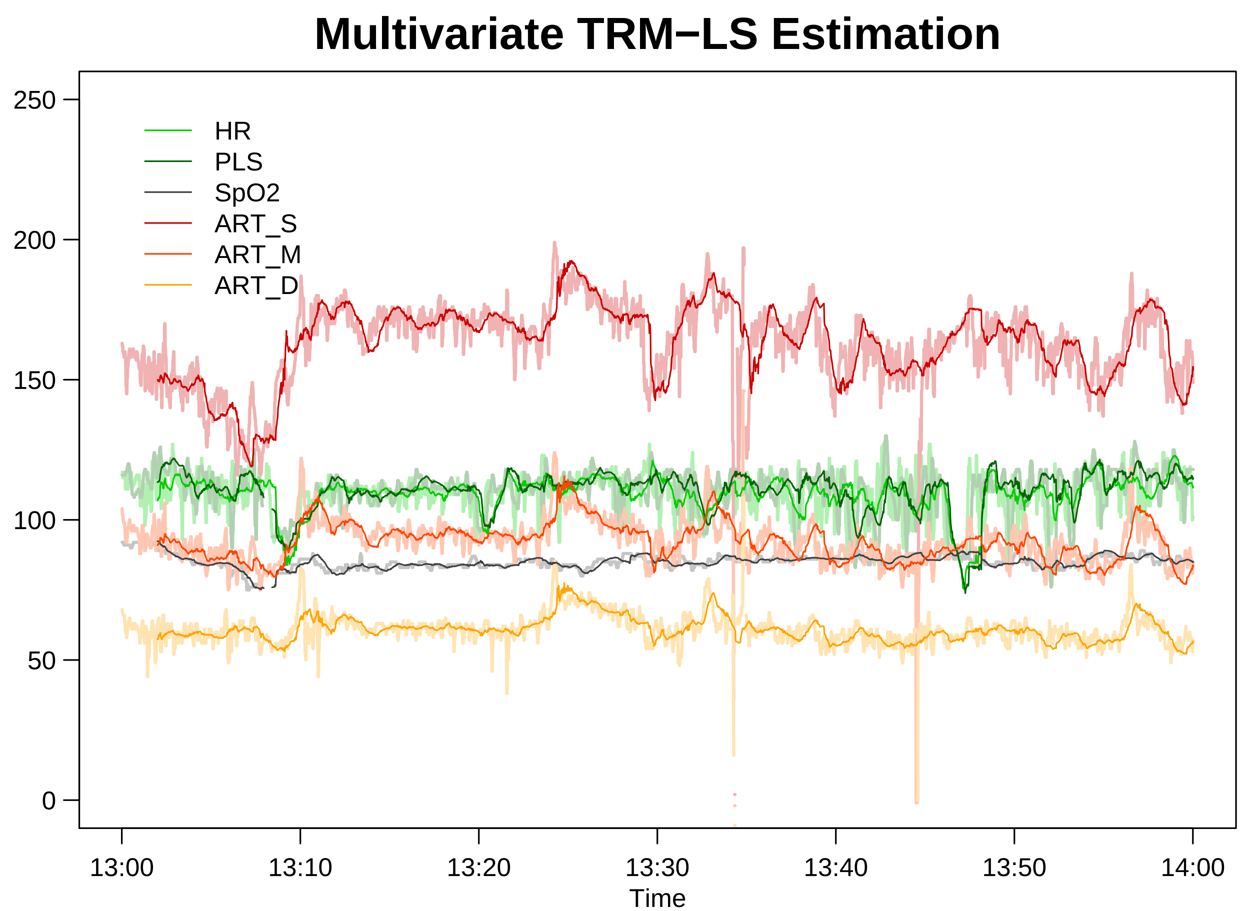
4. Find $I_t = \{\boldsymbol{i = -n(t)+1, \ldots, 0}: \boldsymbol{r}(t+i)^{\mathsf{T}}\hat{\boldsymbol{\Sigma}}(t)^{-1}\boldsymbol{r}(t+i) \leq \boldsymbol{d_{n(t)}}\}$

5. Calculate $\hat{\boldsymbol{\beta}}^{\text{new}}(t)$ and $\hat{\boldsymbol{\mu}}^{\text{new}}(t)$ by Least Squares Regression based on $\{(t+i, \boldsymbol{x}(t+i)), i \in I_t\}$

Comparison: Application to Multivariate Time Series

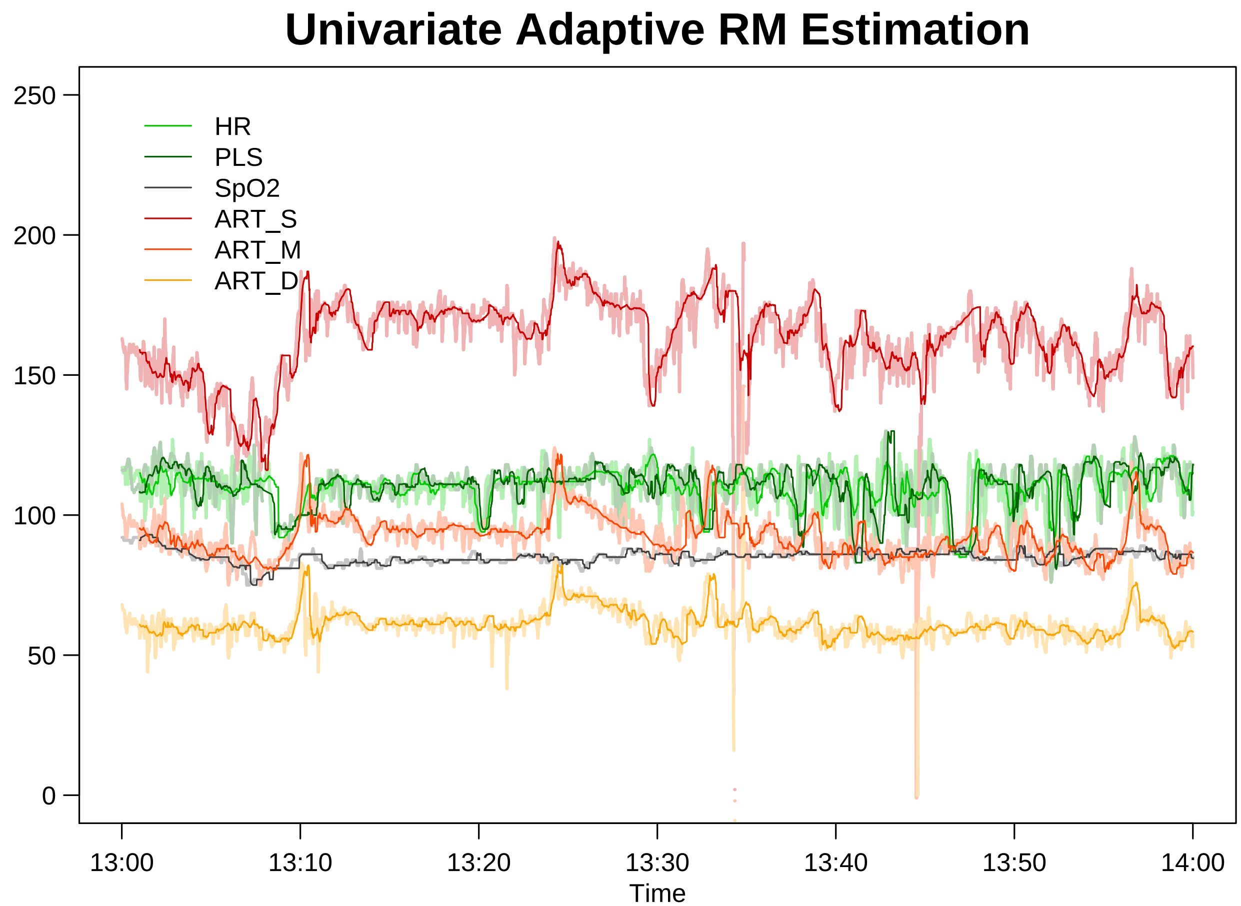


Comparison: Application to Multivariate Time Series



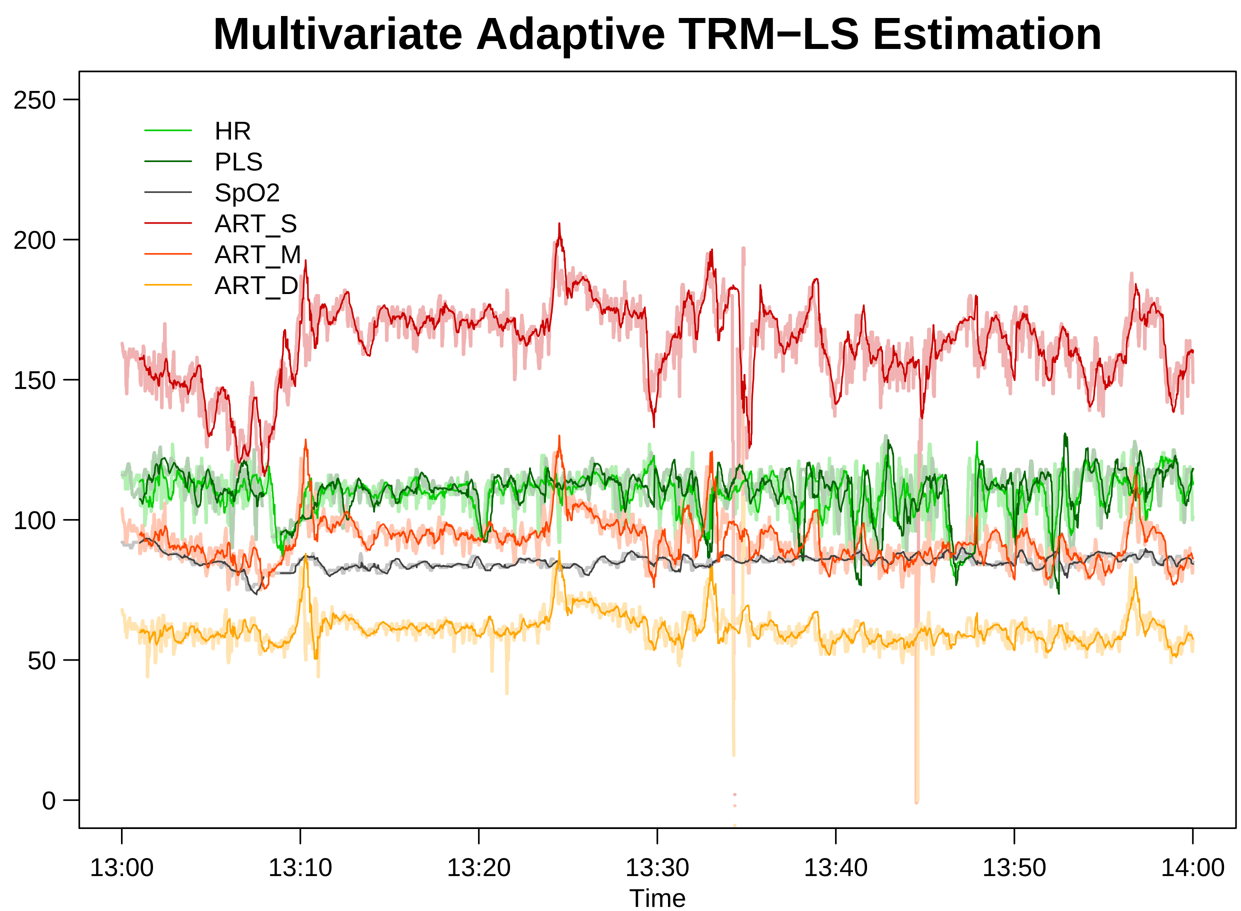
- Smooth
- Large delay at sudden changes and shifts

Comparison: Application to Multivariate Time Series



- Small delay at sudden changes and shifts
- Does not take covariance structure into account

Comparison: Application to Multivariate Time Series



- Small delay at sudden changes and shifts
- Takes covariance structure into account

Summary

- Fast computation
- Robust (50% breakdown point)
- Adapts to sudden changes quickly
- Takes covariance structure into account
- Application to discrete data with missing values possible
- Additional rules against over- / underestimation of the signal

III. Alarm Classification

Intensive Care Data

Physiological variables

- Respiratory rate, oxygen saturation
- Arrhythmia indicator
- Heart rate, pulse
- Arterial systolic, diastolic and mean blood pressure
- Temperature

Thresholds

Alarm information from the monitor (alarm grade)

The Most Frequent Alarms

variable	alarm frequency	without manipulation	
		non alarm relevant	alarm relevant
ART S	1678	602	232
SpO2	1595	491	363
HR	453	311	59
ARR	263	210	15
ART M	268	123	43
RESP	218	168	2

In total: 4747 alarms in 780 hours recording

Consequences of Misclassification

Situation is **alarm relevant** but classified as **non alarm relevant**

$\longrightarrow$ Possibly serious danger to health or life

$\longrightarrow$ Control the probability of misclassifying alarm relevant situations

Consequences of Misclassification

Situation is **alarm relevant** but classified as **non alarm relevant**

→ Possibly serious danger to health or life

→ Control the probability of misclassifying alarm relevant situations

Situation is **non alarm relevant** but classified as **alarm relevant**

→ Annoyance

→ Minimise the probability of misclassifying non alarm relevant situations

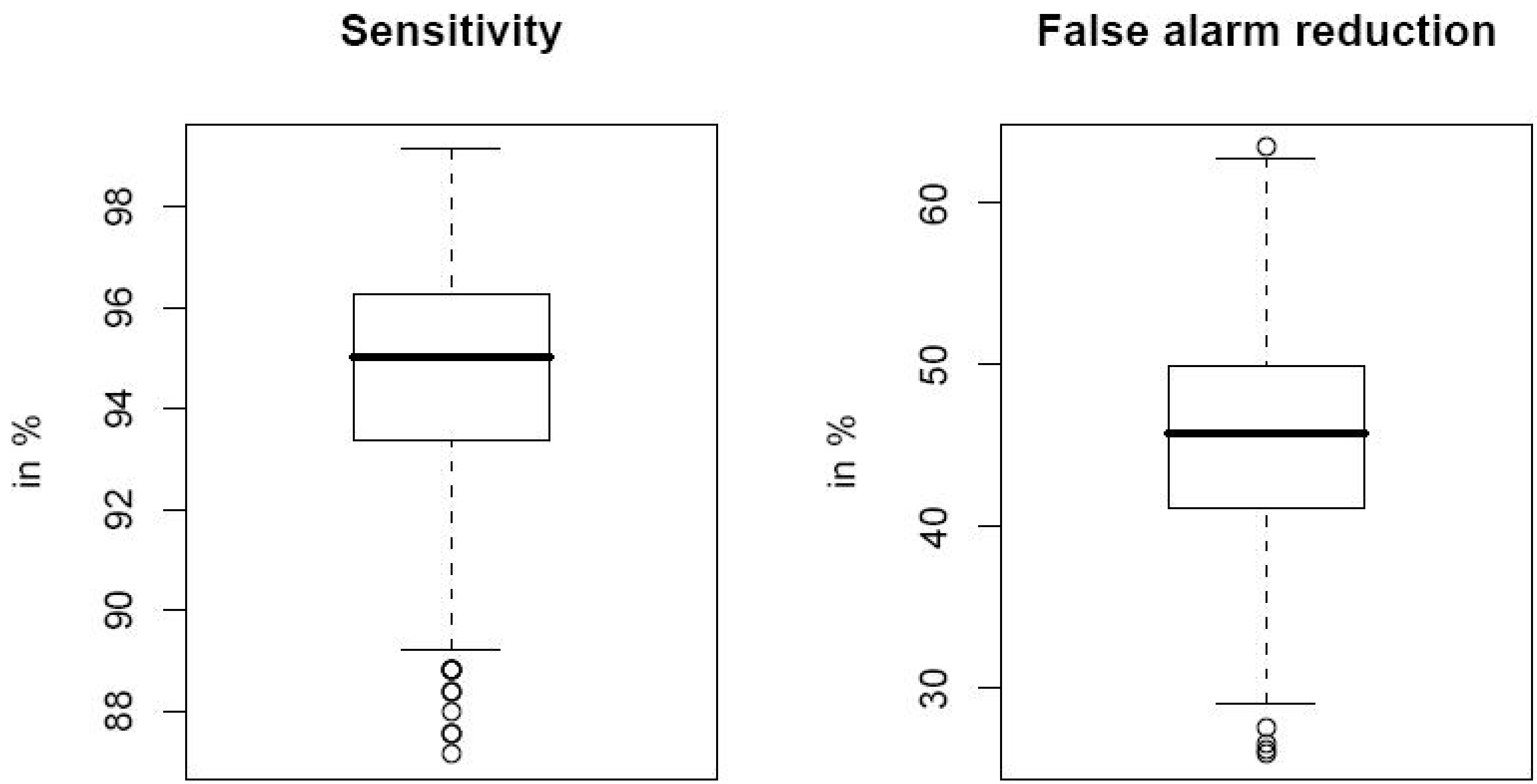
Solution: Random Forest

Construction of a forest (ensemble of decision trees)

- Divide the sample into three sets:
  learning, estimation and test set
- Build a forest of 1000 trees on the learning set
- Estimate the distribution of the test statistic
  on the estimation set
- Find the critical value for the test
- Apply the forest to the test set

➡ Repeat this 1050 times.

Results – Significance Level 5%



Mean sensitivity: **94.7%**

Mean false alarm reduction: **45.6%**

Conclusions and Future Plan

- Combine forests with Repeated Median filtering
- Combine then with alarm delay:
  if decided not to alarm wait 15 seconds and think again

  (Charbonnier, Badji, Gentil, 2005)
- Implement into alarm system

Conclusions and Future Plan

- Combine forests with Repeated Median filtering
- Combine then with alarm delay:
  if decided not to alarm wait 15 seconds and think again
  (Charbonnier, Badji, Gentil, 2005)
- Implement into alarm system

➡ **Intelligent patient monitoring system**

References I

Bernholt, T., Fried, R., Gather, U., Wegener, I. (2006) Modified Repeated Median Filters. *Stat. Comput.* **16**, 177-192.

Borowski, M., Schettlinger, K., Gather, U. (2008) Multivariate Real Time Signal Processing by a Robust Adaptive Regression Filter. *Preprint*, Fakultät Statistik, Technische Universität Dortmund.

Charbonnier, S., Badji, L., Gentil, S. (2005) An Intelligent Alarm System Based on Temporal Episodes for Intensive Care Units. 16th IFAC World Congress, 4-8 July 2005, Prague, Czech republic.

Davies, P.L., Fried, R., Gather, U. (2004) Robust Signal Extraction for On-line Monitoring Data. *J. Stat. Plann. Inference* **122**, 65-78.

Edgeworth, F.Y. (1887) *Metretike or the Method of Measuring Probabilities and Utilities*. London, Temple Company.

Fried, R. (2004) Robust Filtering of Time Series with Trends. *J. Nonparametr. Stat.* **16** (3), 313-328.

Fried, R., Bernholt, T., Gather, U. (2006) Repeated Median and Hybrid Filters. *Comput. Stat. Data An.* **50**, 2313-2338.

Fried, R., Einbeck, J., Gather, U. (2007) Weighted Repeated Median Smoothing and Filtering. *J. Am. Stat. Assoc.*. **102**, 1300-1308.

References II

Fried, R., Schettlinger, K. (2008) `robfilter`: Robust Time Series Filters. R package version 1.0, `http://cran.r-project.org/web/packages/robfilter/`

Gather, U., Schettlinger, K., Fried, R. (2006) Online Signal Extraction by Robust Linear Regression. *Computation. Stat.* **21** (1), 33-52.

Hampel, F.R. (1975) Beyond Location Parameters: Robust Concepts and Methods. *B. ISI* **46**, 375-382.

Lanius, V., Gather, U. (2007) Robust Online Signal Extraction from Multivariate Time Series. *Technical Report 38/2007*, SFB 475, Technische Universität Dortmund.

Rousseeuw, P.J. (1983) Multivariate Estimation with High Breakdown Point. In: W. Grossmann, G. Pflug, I. Vincze, W. Wertz (eds.) *Proc. 4th Pannonian Symp. Math. Statis. Prob.* **B**, D. Reidel, Dordrecht.

Rousseeuw, P.J. (1984) Least Median of Squares Regression. *J. Am. Stat. Assoc.* **79**, 871-880.

Rousseeuw, P.J., Hubert, M. (1999) Regression Depth. *J. Am. Stat. Assoc.* **94**, 388-402.

Schettlinger, K., Fried, R., Gather, U. (2008) Real Time Signal Processing by Adaptive Repeated Median Filters. *Preprint*, Fakultät Statistik, Technische Universität Dortmund.

Siegel, A.F. (1982) Robust Regression Using Repeated Medians. *Biometrika* **69**, 242-244.