Methods and Technologies for Prenatal Cardiac Monitoring

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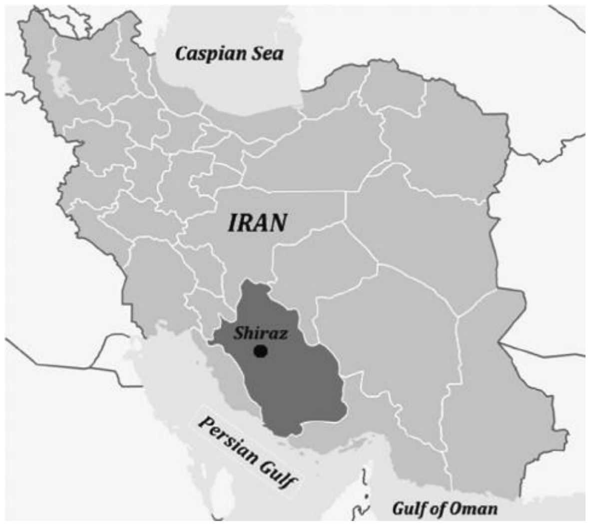
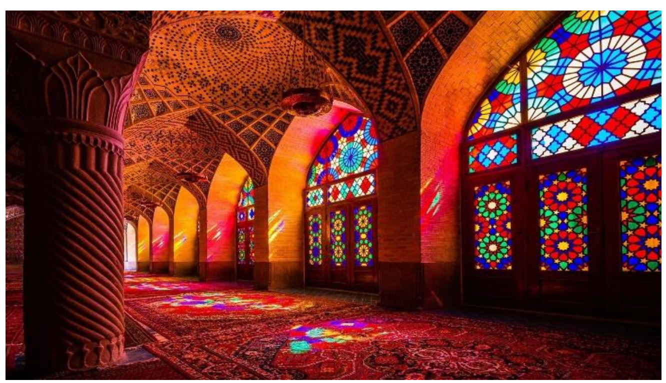
Where I come from…





Where I am…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Brest
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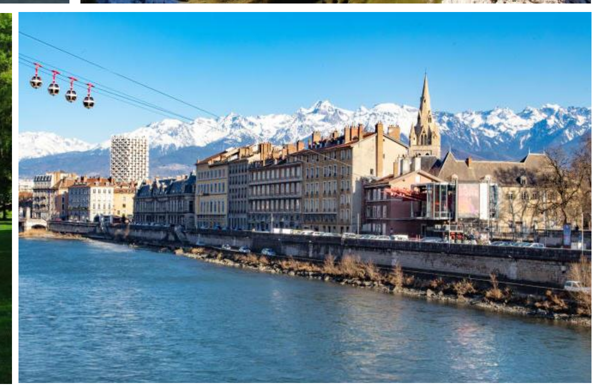


Methods and Technologies for Prenatal Cardiac Monitoring

The lessons we learned from the success story of fetal electrocardiography

Outline

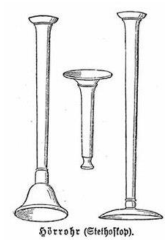
- History of prenatal cardiac monitoring
- Advances in fetal cardiography
- Perspectives

Introduction

History of Prenatal Cardiac Monitoring

Milestones from the Prenatal Cardiac Monitoring Timeline

Cardiac Auscultation



1650 — Marsac heard the fetal heart sound from the maternal abdomen (acknowledged in a French poem by LeGaust)

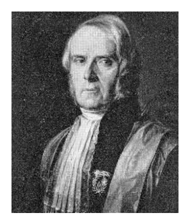
Late 1600s — Killian proposed the relationship between fetal heart-rate and well-being

1816 — Laennec invented mediate auscultation

LAENNEC
(1781–1826)

1818 — Mayer reported the presence of fetal heart sounds when he placed his ear on the maternal abdomen

1819 — Kergaradec used Laennec's stethoscope for fetal cardiac auscultation



KERGARADEC
(1787–1877)

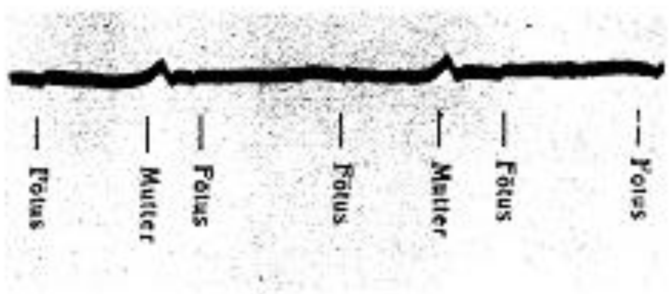
2016 — The first Computing in Cardiology Challenge on heart sound classification (including fetal heart sounds data)

A U.S. Army Reserve nurse uses a Pinard horn in Uganda (2009)

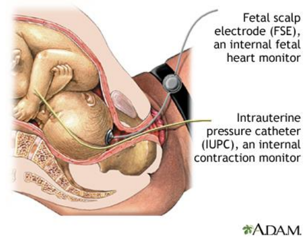
An electronic stethoscope

Milestones from the Prenatal Cardiac Monitoring Timeline

Electrocardiography



The first fetal ECG trace by Cremer



Invasive fetal scalp blood sampling during labor (Saling, 1964)

Cremer recorded the first fetal ECG using abdomino-vaginal and abdomino-rectal leads

Noninvasive fetal ECG enhancement by signal processing

The first clinical noninvasive fetal ECG monitors

1901 | 1906 | 1940s | 1960s | 1970s | 1990s | 2010 onwards

Einthoven recorded the first ECG by string galvanometer

The beginning of the digital electronics and signal processing era

Development of multichannel blind source separation algorithms

Improvements in measurement and amplification techniques

Development of the SQUID technology

Fetal Magnetocardiography

Milestones from the Prenatal Cardiac Monitoring Timeline

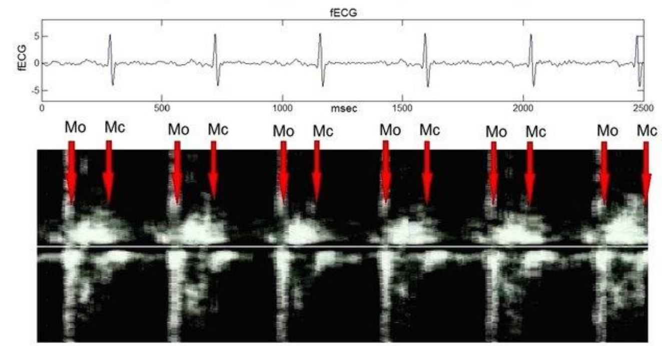
Cardiotocography

1940s — Early Doppler technologies

Early 1960s — The use of electronic methods for acquiring and recording fetal heart rate (FHR) and uterine contraction (UC) by Hon, Caldeyro-Barcia, and Hammacher

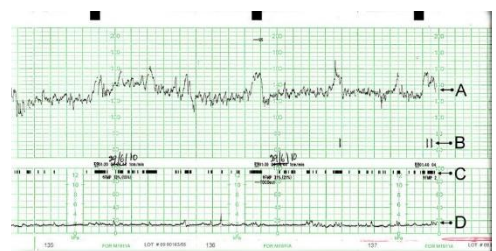
1968 — The first commercial fetal monitor by Hammacher and Hewlett-Packard

The first fetal CTG monitor by Hewlett-Packard 8020A



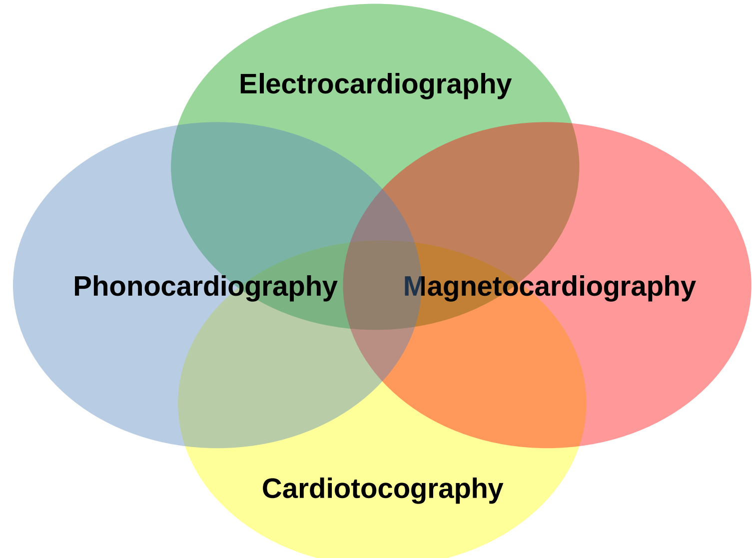
2010 onwards

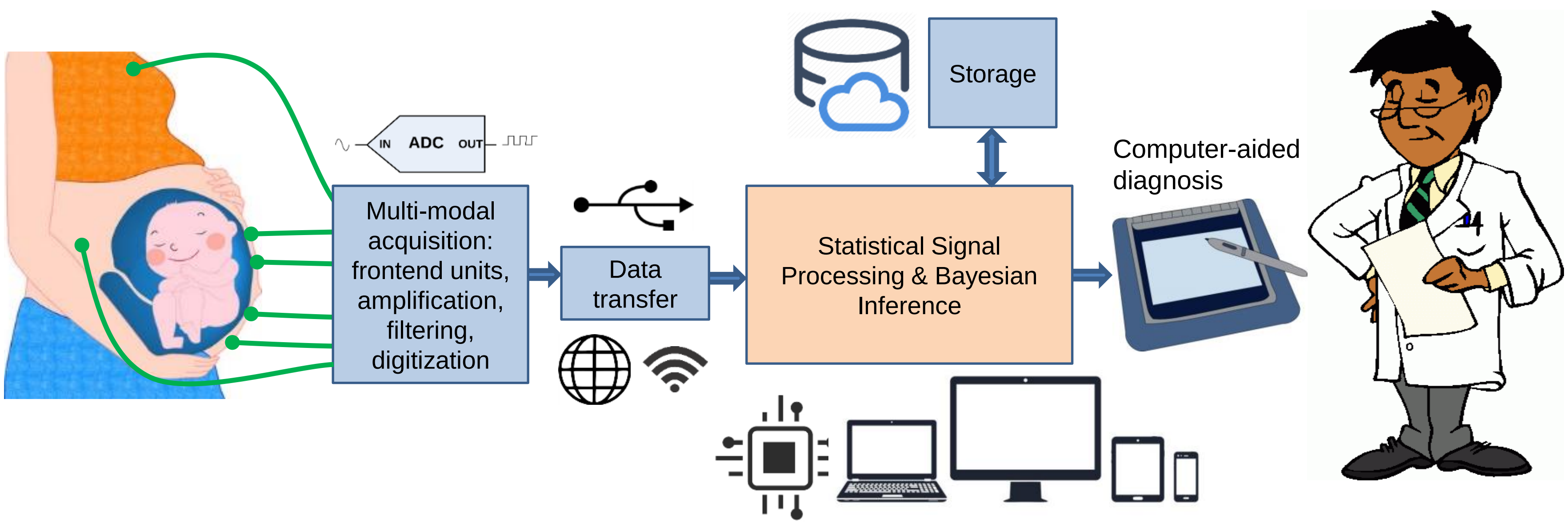
- Low-price 1D Doppler for home monitoring
- Multimodality (Simultaneous fECG and Doppler)



Research & Technology Trend

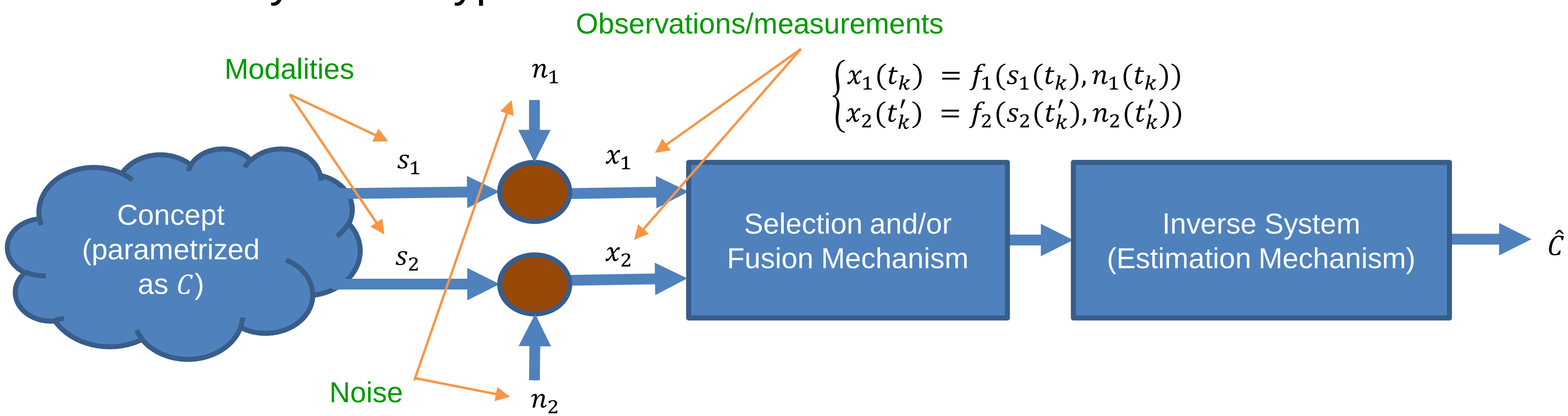
- Prenatal care has always benefitted from latest technologies of the era (stethoscopy, galvanometry, electronics, Doppler ultrasound, signal processing, SQUID, etc.)
- Emerging technology: Multimodal and Hyper-modal prenatal monitors





Multimodality

- Multimodality has vast applications in biomedical data, where a physiological concept is observed/monitored through parameters obtained by different modalities (measurement systems).
- Each modality covers certain aspects of the concept, at some level of abstraction
- Different modalities may partially overlap with and complement one another
- The Multimodality Stereotype:

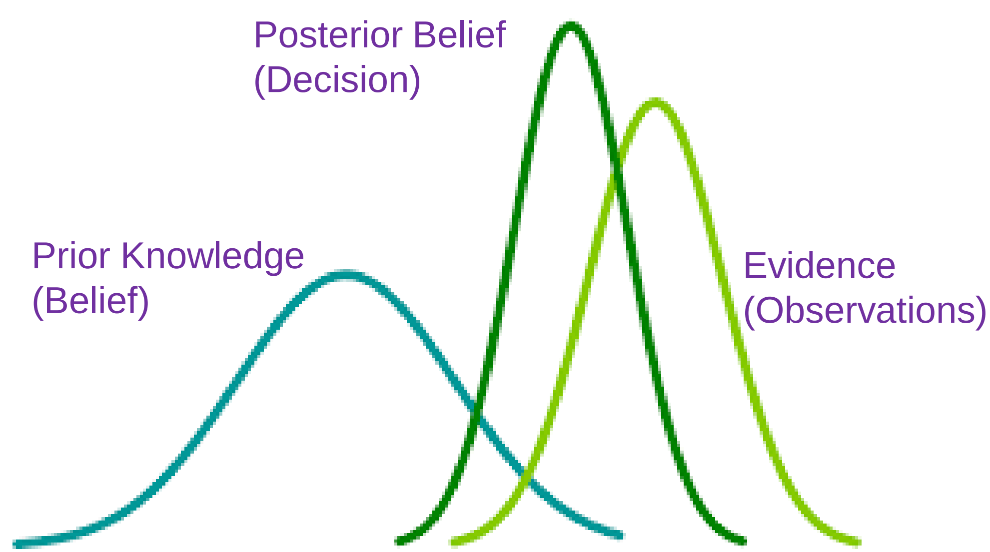


- Objective: Multimodality is used to obtain more knowledge of the concept of interest and to extract its parameters more precisely, using the modality overlaps, diversities, synergies and innovations.
- Issues: Noise, mismatch/inconsistency, alignment, lags, missing segments, etc.

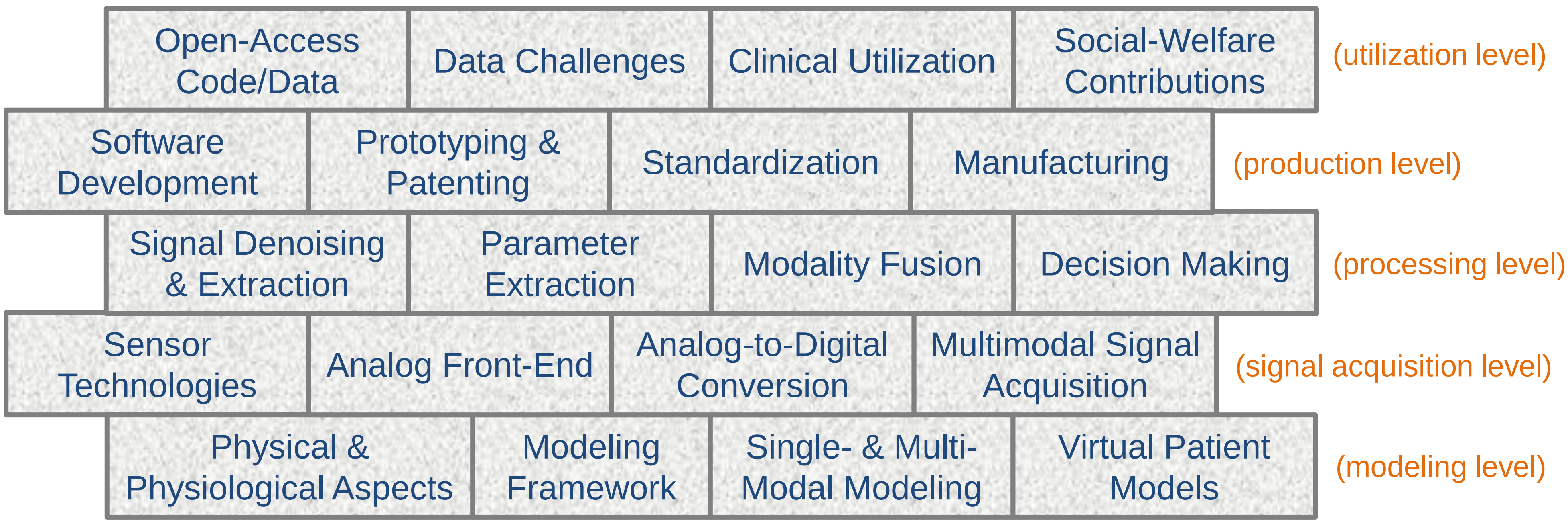
Hyper-Modality

- Our Definition: The fusion of multiple modalities as a unified Hyper-modality, using statistical signal processing, machine learning and Bayesian inference
- Hyper-modality can be eventually represented in an *ad hoc* multimedia (audio-visual) form, acceptable for clinicians (like CTG sounds, MRI, CT, etc.)
- Why use a Bayesian framework?

Bayesian Inference = Model + Observations + Signal/Noise Priors



Requirements of Hyper-Modal Prenatal Monitoring



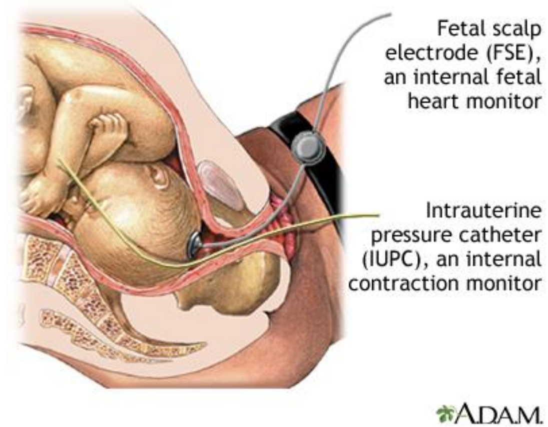
The Open-Source Electrophysiological Toolbox (OSET)

- OSET (www.oset.ir) is a collection of electrophysiological data and open source codes for biological signal generation, modeling, processing, and filtering, originally released in 2006.
- It is distributed under the GNU General Public License and may be freely used or modified under the specified terms of use.
- The source codes have been mainly developed in Matlab and partially in C++; but contributions in other languages are welcome.
- Starting from Version 3.14 (the π version), OSET is accessible and will be updated on a Git repository (https://gitlab.com/rsameni/OSET.git)

Electrophysiological aspects of fetal electrocardiography

Fetal ECG Recording Methods

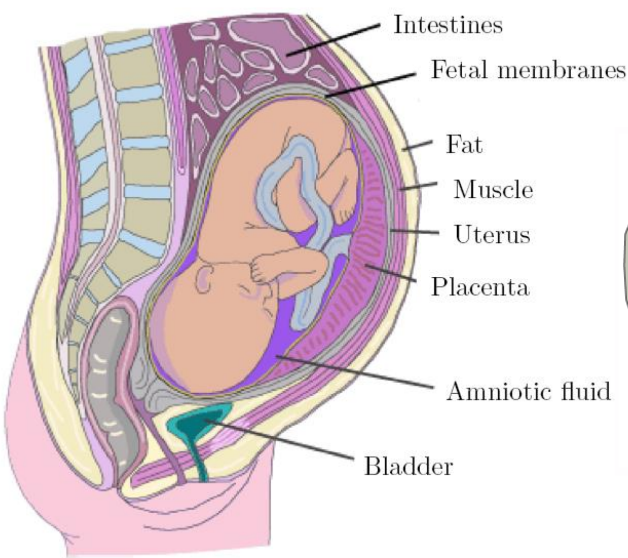
- Invasive (Direct) Methods: Fetal scalp electrode; used in normal vaginal deliveries during labor after amniotic sac (fluid) rupture, to identify fetuses at risk of hypoxia (oxygen deficiency) during labor

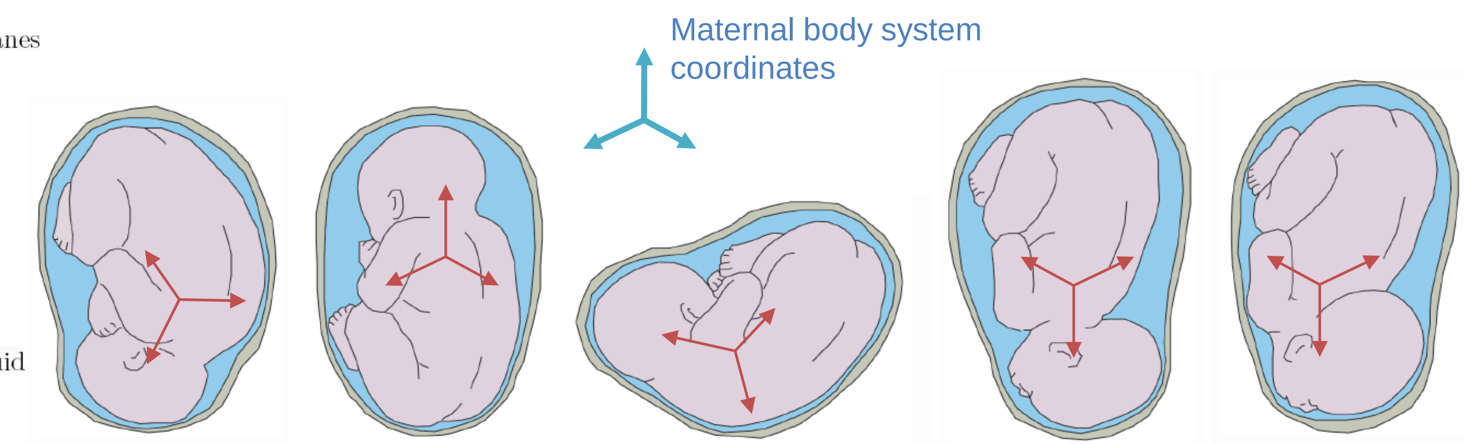


- Noninvasive (Indirect) Methods: Recorded noninvasively from maternal abdominal leads

Physiological Issues

- Weakness of fetal cardiac signals
- Strong maternal ECG and respiration interference
- The fetal body coordinates varies with fetal movements and rotations with respect to the maternal body coordinates (and the surface leads)
- Electrode positioning
- Multiple pregnancies (twin, triplet, ...)
- Electrically insulating layers such as the *vernix caseosa*





The Physics of Noninvasive Fetal ECG

Physical properties of the volume conductor between the fetal heart and the maternal body surface:

1. Linear: superposition holds for the electrical potentials of the sources (mother; fetuses; etc.).
2. Time-variant: modulating effects on the fECG (due to maternal respiration) and the fetal motion
3. Negligible electric displacement current: the electromagnetics is quasi-static
   - The electric and magnetic fields are decoupled
   - The electric field is proportional to the gradient of electric scalar potentials
   - The divergence of the current density is zero
4. Negligible capacitive effect: the tissues are with a very good approximation resistive (due to low frequency)
5. Spatially distributed source: it can only be approximated by a dipole in the far-field

Further Reading: D. B. Geselowitz, On the Theory of the Electrocardiogram," Proc. IEEE, vol. 77, pp. 857-876, Jun. 1989.

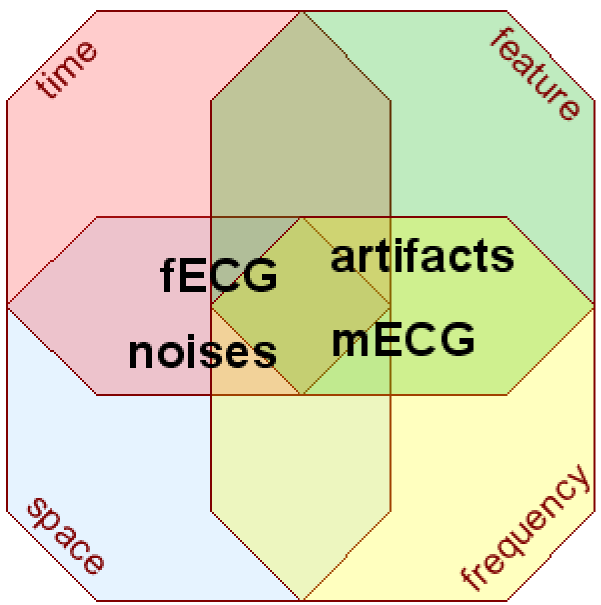
Major Fetal ECG Noises and Interferences

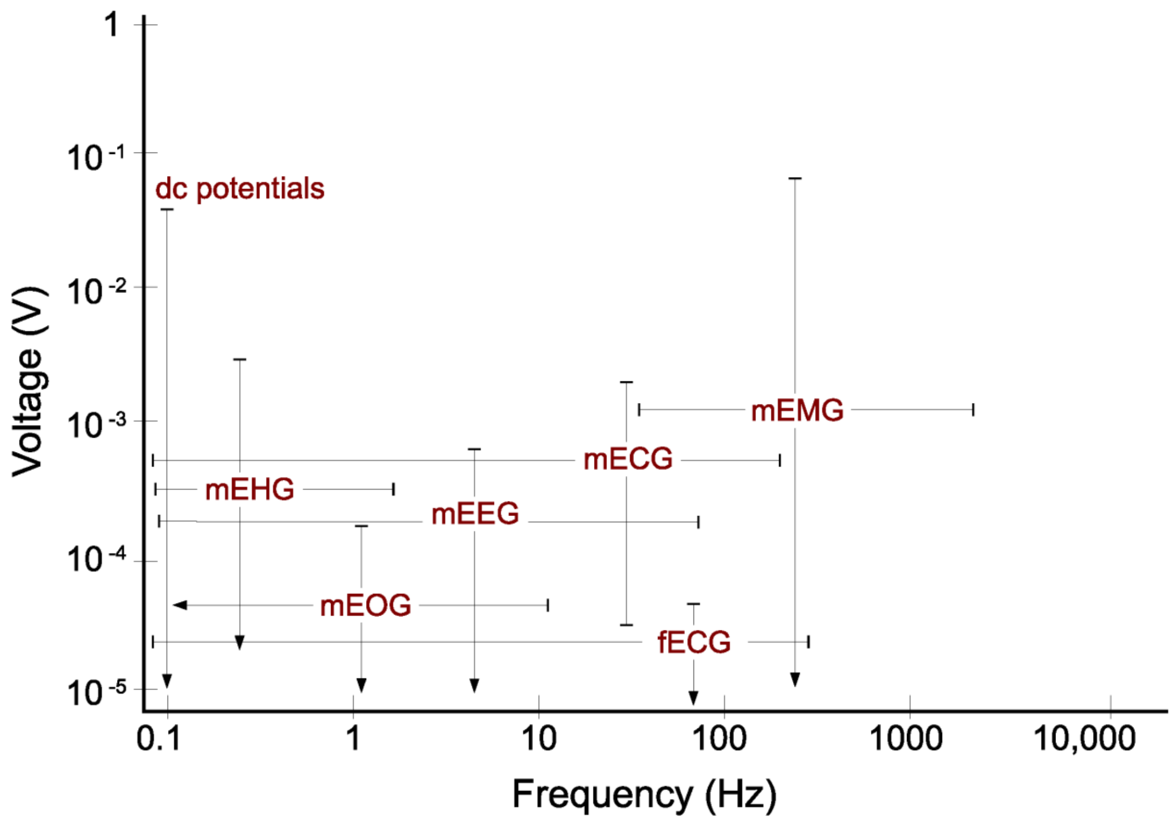
In addition to the intrinsic fetal ECG noted above:

- Maternal interferences:
  - ECG (the major interference)
  - Uterus and muscle contractions
  - Baseline wander due to maternal respiration
- Device noises (inductive and conductive):
  - Power-line noise
  - Bedside monitors
  - Infusion pumps
  - Cellphones
  - USB devices
  - etc.
- Other fetal interferences: in multiple pregnancies

Major Fetal ECG Noises and Interferences (continued)

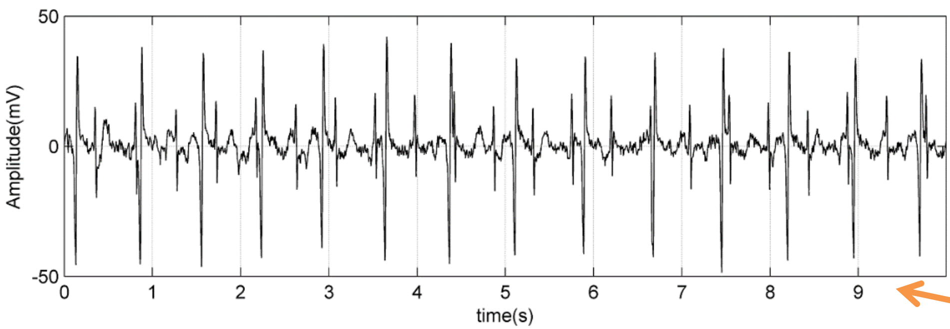
- The noises and interferences overlap with the fECG in all domains

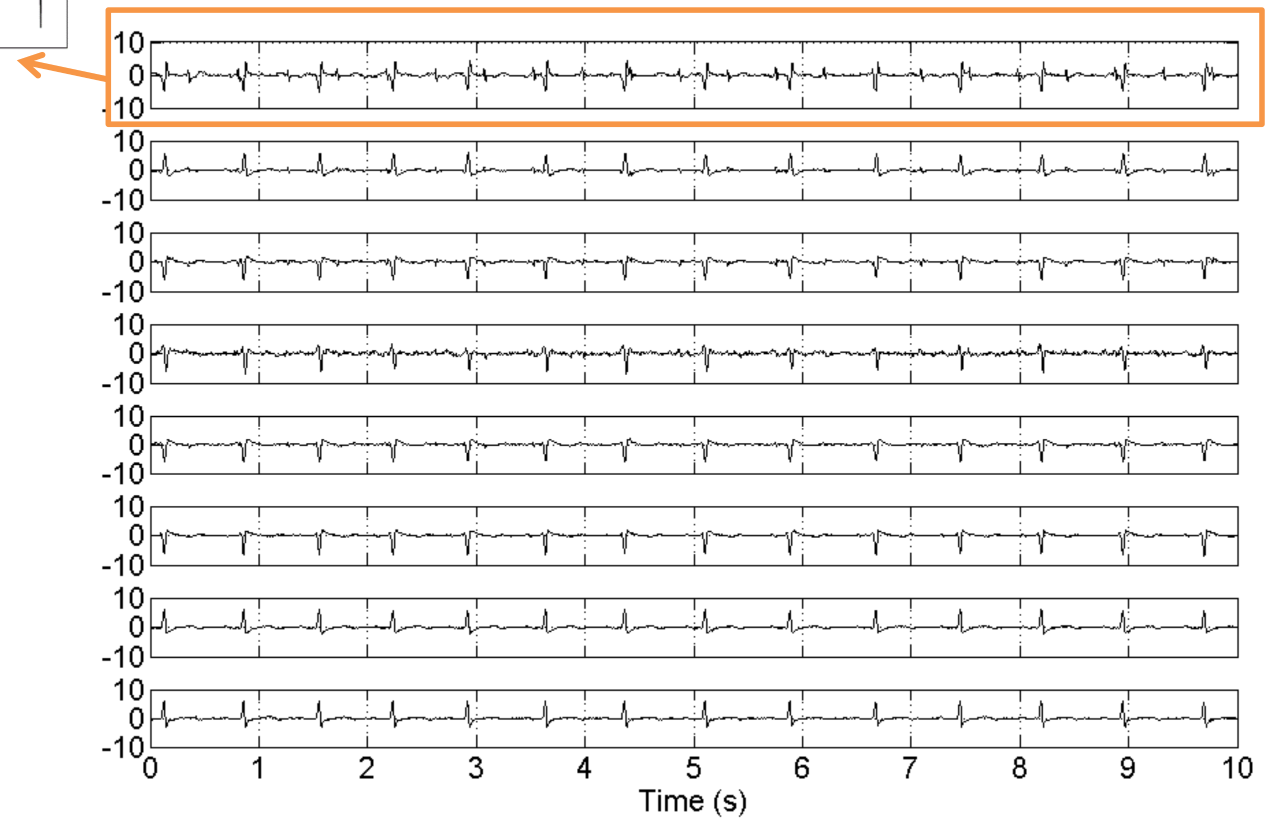




Typical Fetal ECG Samples

Example 1: The DaISy dataset





B. De Moor, Database for the Identification of Systems (DaISy), 1997. [Online]. Available: http://homes.esat.kuleuven.be/~smc/daisy/

Typical Fetal ECG Samples

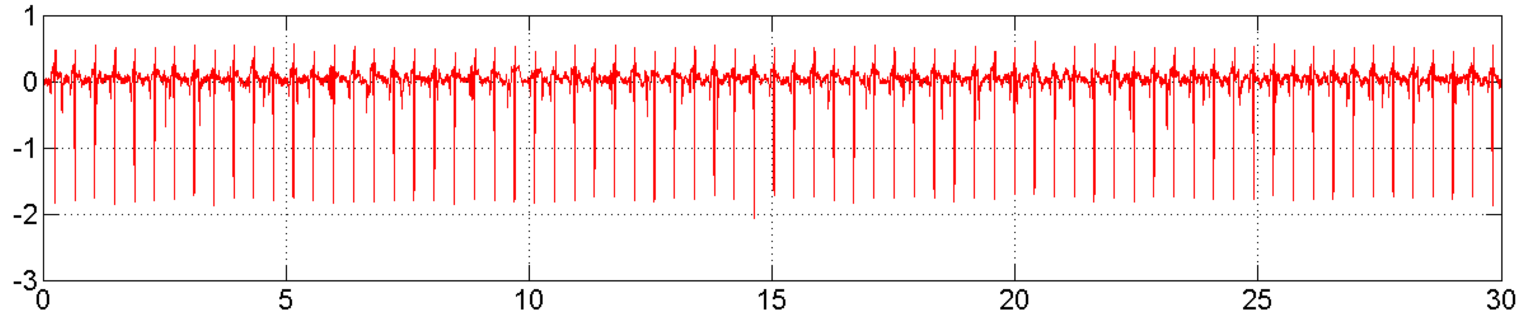
Example 2: Six-channel fetal ECG

Sample data recorded by Dr. Evelyn Huhn and provided by Dr. Raphael Schneider

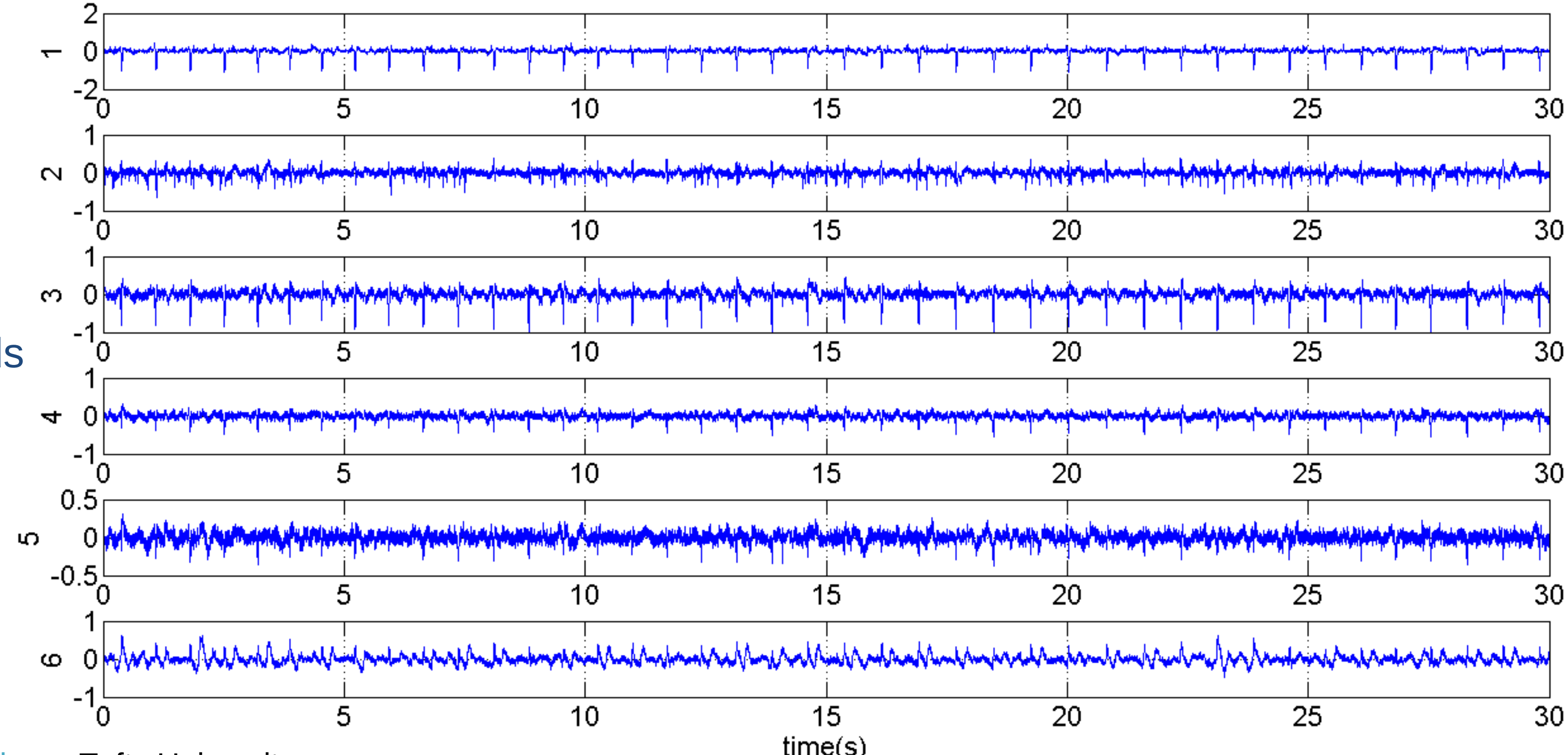
Typical Fetal ECG Samples

Example 3:

Fetal scalp lead



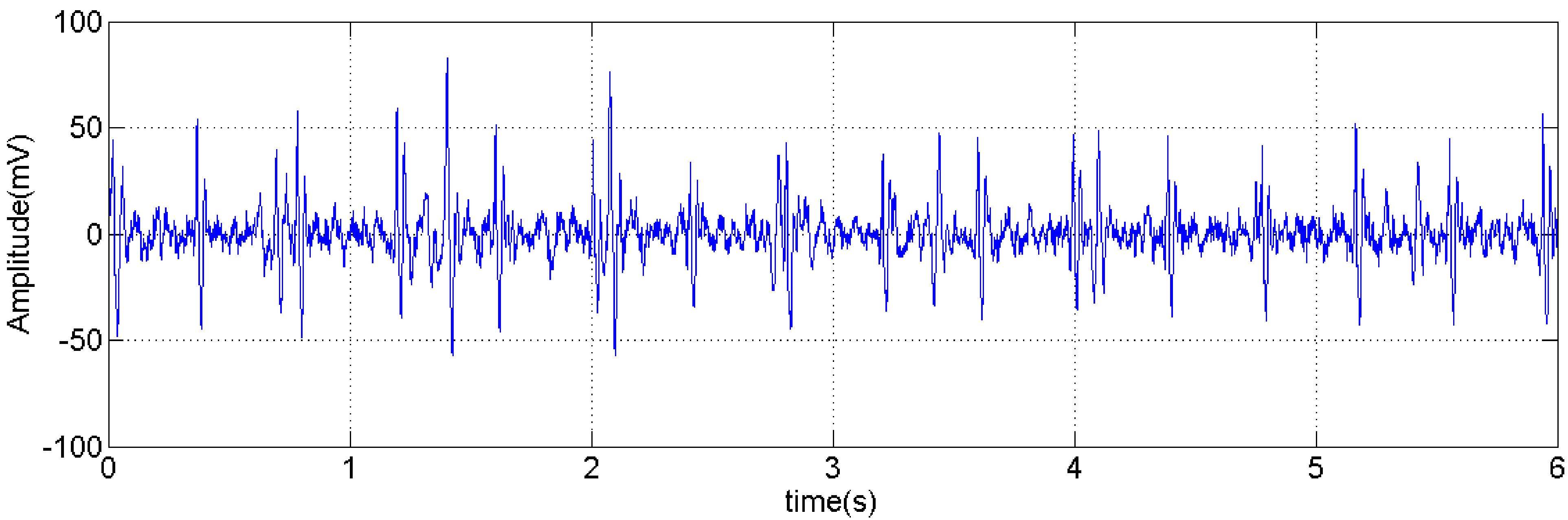
Maternal abdominal leads



Sample data provided by Dr. Adam Wolfberg, Tufts University

Typical Fetal ECG Samples

Example 4: Notice the maternal peaks among the fetal peaks

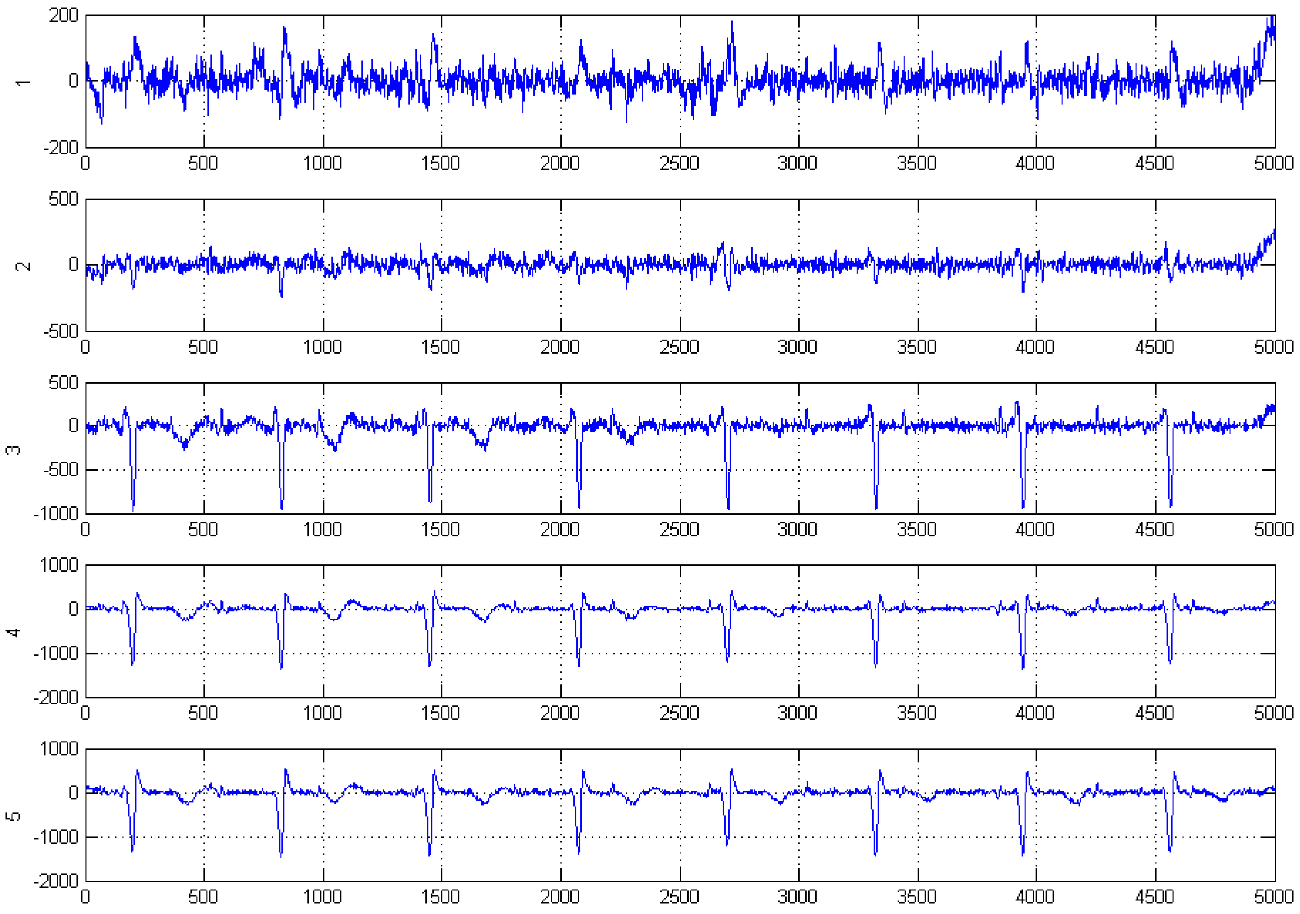


A sample data from the PhysioNet fetal ECG database

Typical Fetal MCG Samples

Example 5: Twin MCG recordings (5 out of 168 channels)

Morphologically resembles the ECG



Sample data provided by Dr. Dirk Hoyer, Jena University

Open-Access Code/Data
Data Challenges
Clinical Utilization
Social-Welfare Contributions

Software Development
Prototyping & Patenting
Standardization
Manufacturing

Signal Denoising & Extraction
Parameter Extraction
Modality Fusion
Decision Making

Sensor Technologies
Analog Front-End
Analog-to-Digital Conversion
Multimodal Signal Acquisition

Physical & Physiological Aspects
Modeling Framework
Single- & Multi-Modal Modeling
Virtual Patient Models

Mathematical Modeling

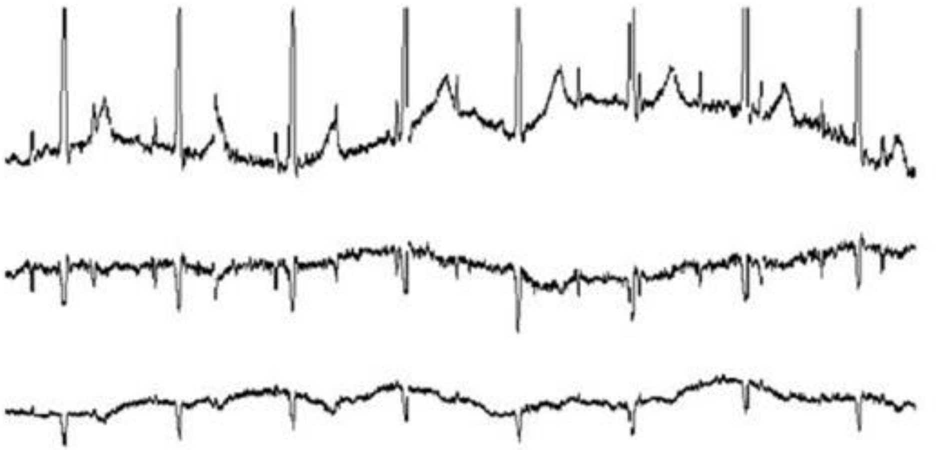
Maternal Abdominal Signal Model

A linear model

$$x(t) = x_m(t) + x_f(t) + n(t)$$

$$x_m(t) = \sum_k s_m(t - t_k; \theta_k)$$

$$x_f(t) = \sum_l s_f(t - u_l; \varphi_l)$$

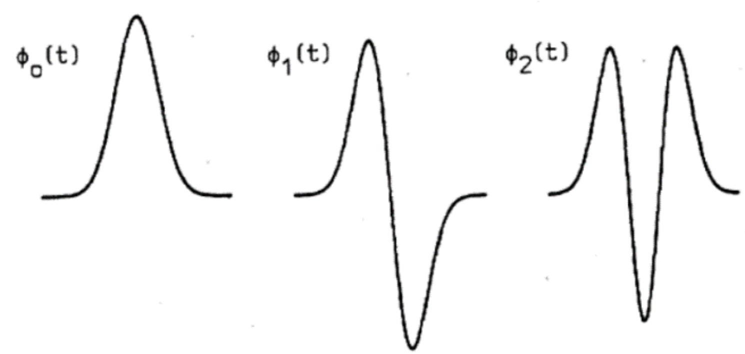


- $x(t)$: maternal abdominal measurement
- $x_m(t)$: maternal ECG noise on abdominal lead
- $x_f(t)$: fetal ECG recorded from the abdominal lead
- $s_m(t)$: a single maternal ECG beat
- $s_f(t)$: a single fetal ECG beat
- t_k: the maternal R-peak locations in time
- u_l: the fetal R-peak locations in time
- θ_k: beat-wise variable maternal ECG morphologic parameters
- φ_l: beat-wise variable fetal ECG morphologic parameters
- $n(t)$: measurement noise

For fetal ECG extraction, we face a model-based filter design problem

Morphologic ECG Models

- Motivation: Mathematical modeling of the ECG waveform has applications in ECG test instruments and pedagogy
- Adult ECG modeling:
  - Scher et al. (1960) ▶ Factor analysis
  - Sornmo et al. (1981) ▶ Bessel functions
  - Laguna et al. (1996) ▶ Hermite polynomials
  - McSharry et al. (2003) ▶ Gaussian kernels in a dynamic fc
- Fetal ECG modeling:
  - Oostendorp (1989) ▶ Finite element
  - Sameni et al. (2007) ▶ Dynamic form



McSharry-Clifford's model became a turning point in ECG modeling and analysis; due to its dynamic representation

Fetal ECG modeling: T. Oostendorp, *Modeling the Fetal ECG*. Ph.D. dissertation, K. U. Nijmegen, The Netherlands, 1989

McSharry-Clifford's Synthetic ECG Generator and its Polar Extension

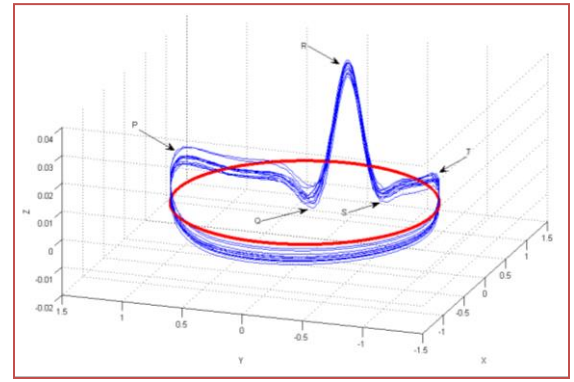
A dynamic model of the ECG using sum of Gaussian functions:

$$\begin{cases} \dot{x} = \rho x - \omega y \\ \dot{y} = \rho y + \omega x \\ \dot{z} = -\sum\limits_{i \in \{P,Q,R,S,T\}} a_i \Delta\theta_i exp(-\frac{\Delta\theta_i^2}{2b_i^2}) - (z - z_0) \end{cases}$$

$$\rho = 1 - \sqrt{x^2 + y^2}$$

$$\theta = atan2(y, x)$$

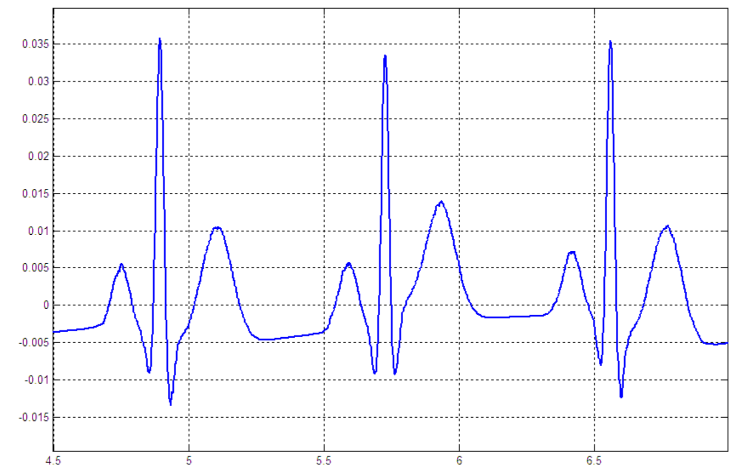
$$\Delta\theta_i = (\theta - \theta_i) mod(2\pi)$$



3D trajectory of the model

$$\begin{cases} \theta_{k+1} = (\theta_k + \omega\delta) mod(2\pi) \\ z_{k+1} = -\sum\limits_i \delta \frac{\alpha_i \omega}{b_i^2} \Delta\theta_i exp(-\frac{\Delta\theta_i^2}{2b_i^2}) + z_k + \eta \end{cases}$$

$$\Delta\theta_i = (\theta_k - \theta_i) mod(2\pi)$$



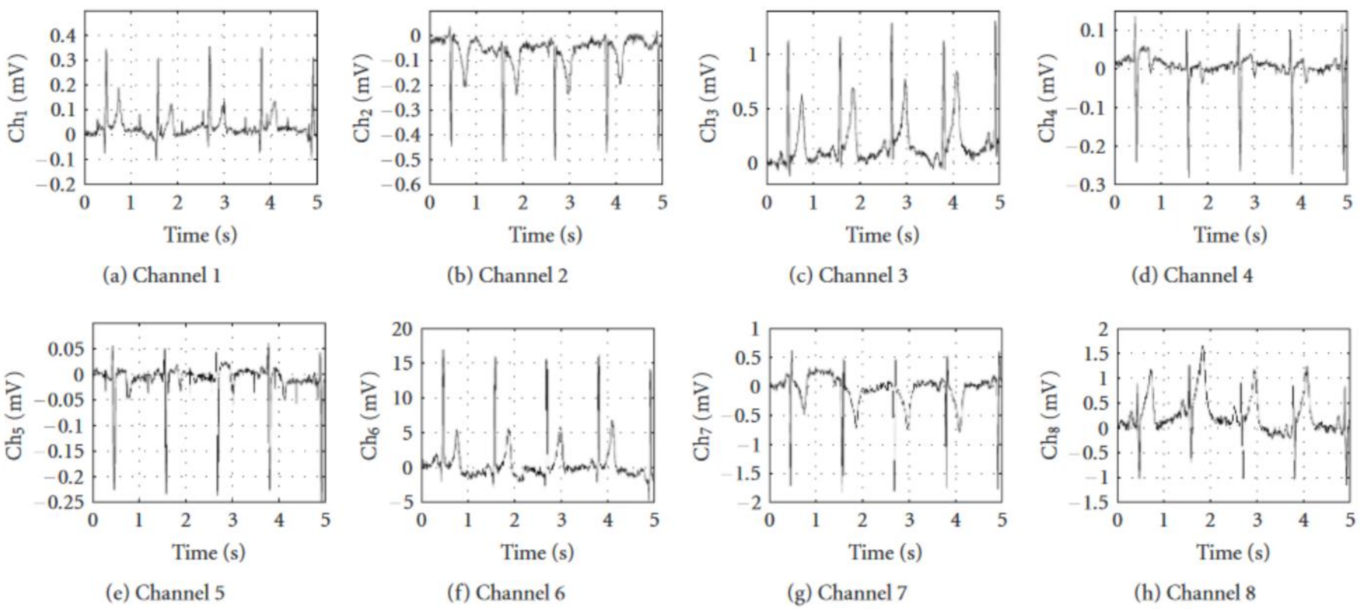
A sample synthetic ECG

Ref:

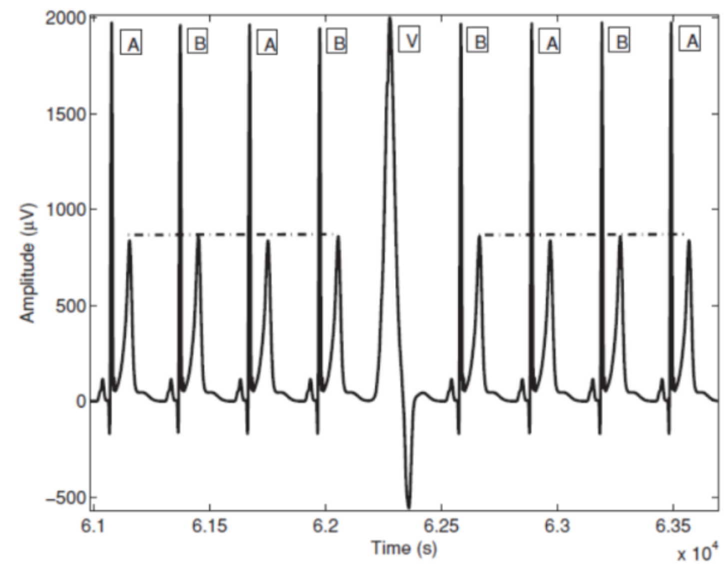
- P.E. McSharry, et al. "A dynamical model for generating synthetic electrocardiogram signals" IEEE Transactions on Biomedical Engineering 50.3 (2003): 289-294.
- R. Sameni, et al. "Filtering noisy ECG signals using the extended Kalman filter based on a modified dynamic ECG model." Computers in Cardiology, 2005. IEEE, 2005.

Extensions of McSharry-Clifford’s Model

- McSharry-Clifford’s ECG model was further extended to
  - Multichannel adult and fetal VCG and ECG
  - Normal versus abnormal ECG with ectopic beats



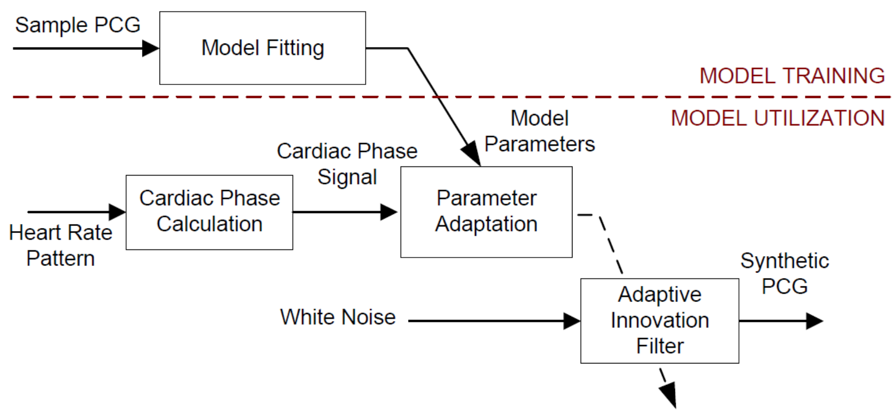
(Sameni et al. 2007)



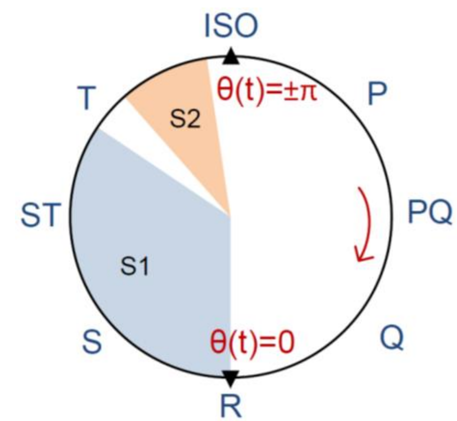
(Clifford et al. 2010)

Phonocardiogram Modeling

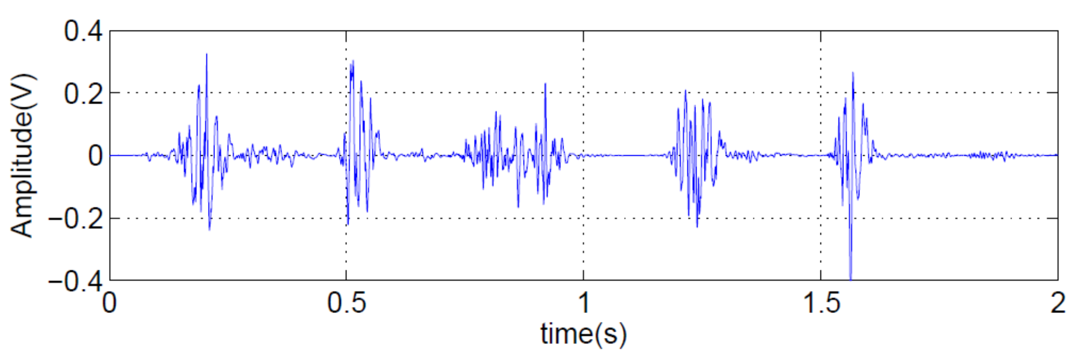
A simultaneous ECG-PCG model



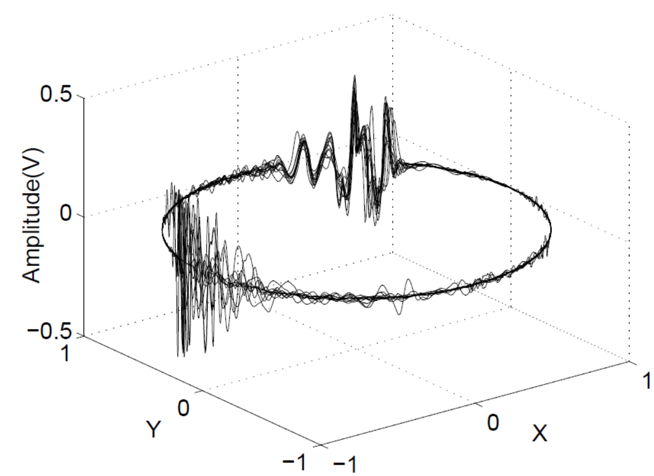
An acoustic PCG model synchronous with the ECG



The ECG vs PCG cardiac cycle



Synthetic PCG



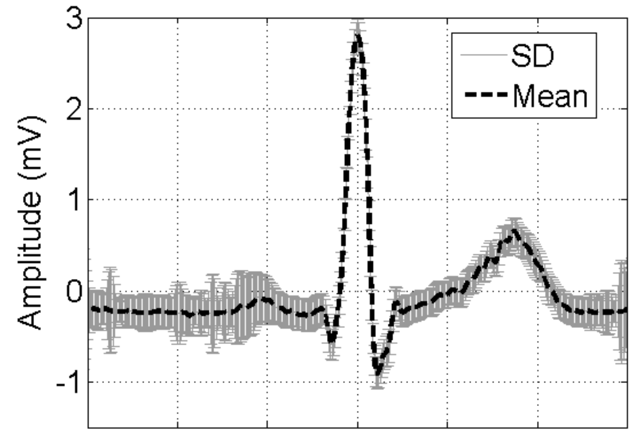
Phase-wrapped PCG

Statistical Performance Bounds on ECG Parameter Estimation

Objective: To find theoretical bounds for the performance of ECG parameter estimation (Heartrate, QT interval, ST-level, T/R ratio, etc.)

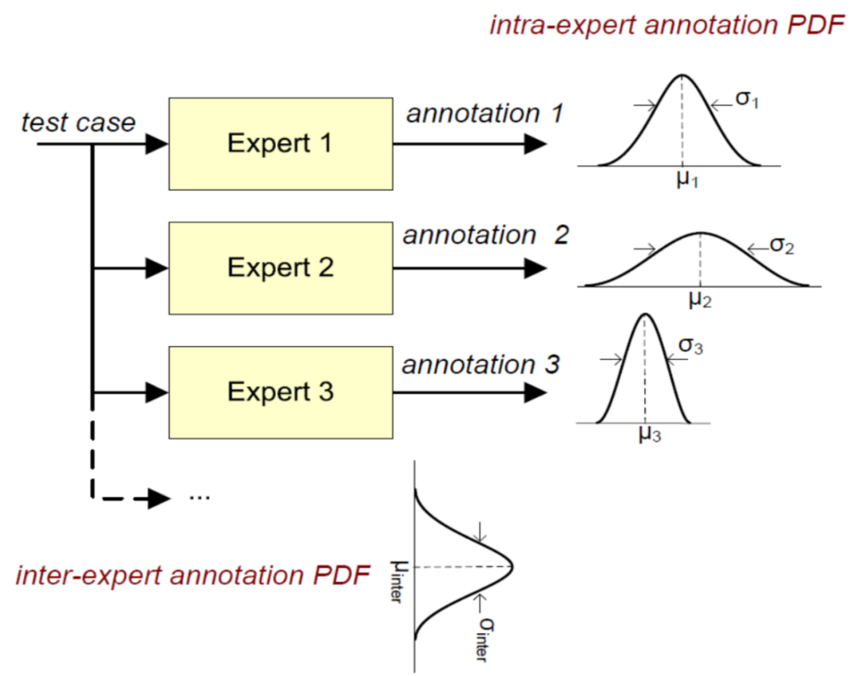
Facts:

- ECG parameter extraction is implicitly/explicitly model-based
- ECG parameters have intrinsic beat-wise variability ► *modeling errors*
- Measurements and expert annotations are always noisy, with inter-rater and intra-rater variabilities ► *observation noise*



Result: We derived Cramér–Rao Lower Bounds (CRLB) of ECG parameters for the most popular ECG models (orthogonal bases, polynomials, and sum of Gaussians).

The results do not depend on the parameter estimation method; but only rely on the presumed data model.



- Ref: Current research by D. Fattahi (PhD candidate) in Shiraz University, 2019
- Related research: Zhu, T., Johnson, A. E., Behar, J., & Clifford, G. D. (2014). Crowd-sourced annotation of ECG signals using contextual information. *Annals of biomedical engineering*, *42*(4), 871-884.

Maternal ECG cancellation and denoising

Maternal ECG Cancellation

- Methods used for maternal ECG cancellation and denoising
  - Template subtraction: Ordinary vs. robust weighted averaging
  - Multichannel projection: PCA, SVD, VCG alignment, weighted least squares
  - Neural Networks: Multilayer perceptrons
  - Adaptive filters: Recursive least squares, etc.
  - Bayesian filters: Extended Kalman filters, H-infinity filters

Further reading:

- J. Leski,“Robust weighted averaging [of biomedical signals],”IEEE Trans. Biomed. Eng., vol. 49, no. 8, pp. 796–804, 2002.
- N. V. Thakor and Y. S. Zhu, “Application of adaptive filtering to ECG analysis: noise cancellation and arrhythmia detection,” IEEE Trans. Biomed. Eng., vol. 38, pp. 785–794, 1991.
- L. Sornmo, “Vectorcardiographic loop alignment and morphologic beat-to-beat variability,” Biomedical Engineering, IEEE Transactions on, vol. 45, no. 12, pp. 1401–1413, December 1998.
- M. Astrom, E. Santos, L. Sornmo, P. Laguna, and B. Wohlfart, “Vectorcardiographic loop alignment and the measurement of morphologic beat-to-beat variability in noisy signals,” Biomedical Engineering, IEEE Transactions on, vol. 47, no. 4, pp. 497–506, April 2000
- Vullings, R., Peters, C. H. L., Mischi, M., Oei, S. G., & Bergmans, J. W. M. (2008, August). Fetal movement quantification by fetal vectorcardiography: a preliminary study. In *Engineering in Medicine and Biology Society, 2008. EMBS 2008. 30th Annual International Conference of the IEEE* (pp. 1056-1059). IEEE

A Kalman Filter for ECG Denoising

Dynamical models of the ECG can be used to design a Kalman filter (or extended Kalman filter) for ECG denoising:

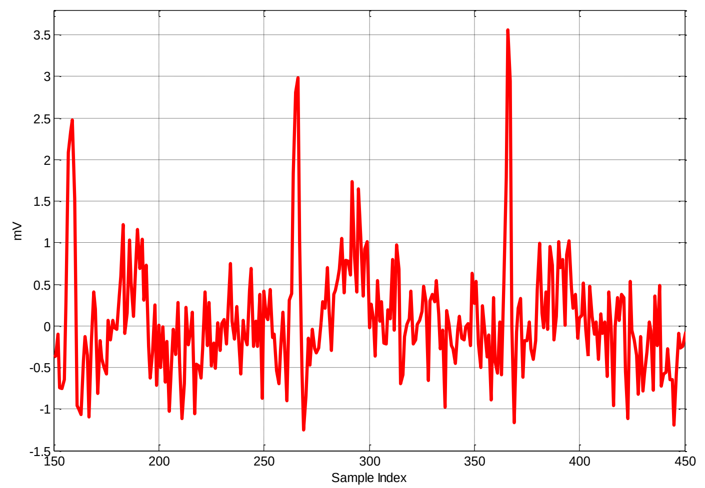
Process equation:

$$\begin{cases} \theta_{k+1} = (\theta_k + \omega\delta) mod(2\pi) \\ s_{k+1} = -\sum_{i=1}^{N} \delta \frac{\alpha_i \omega}{b_i^2} \Delta\theta_i exp(-\frac{\Delta\theta_i^2}{2b_i^2}) + s_k + \eta \end{cases}$$

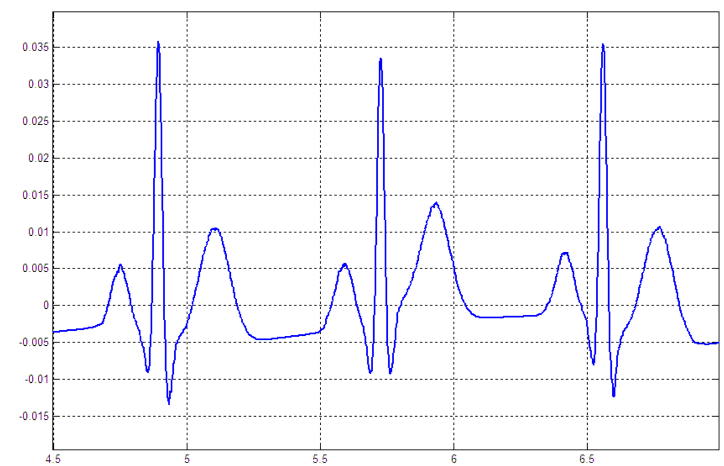
Dynamical ECG model

Observation equation:

$$\begin{cases} \phi_k = \theta_k + u_k \\ y_k = s_k + v_k, \end{cases}$$

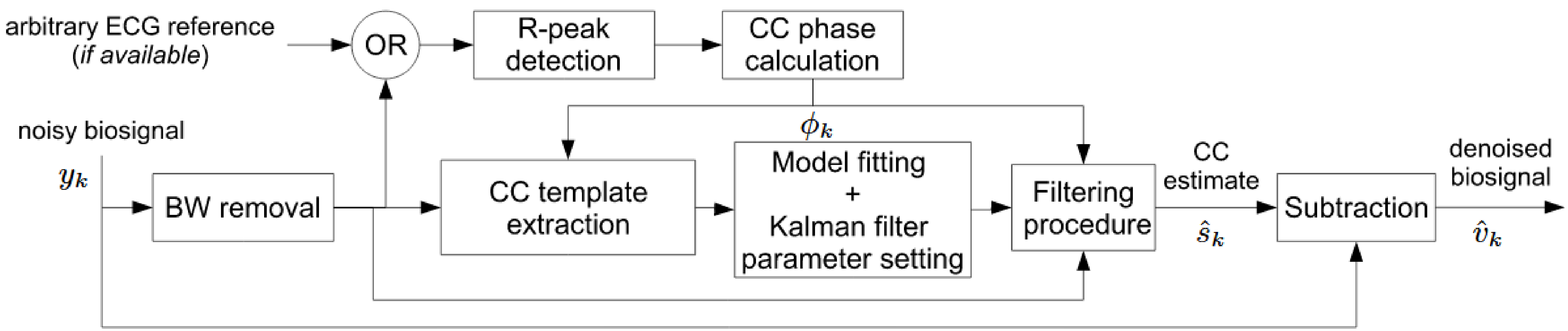


Noisy observations



Maternal ECG Cancellation using Extended Kalman Filters

- For our application of interest, the noted Kalman filtering scheme can be used to adaptively remove the mECG from maternal abdominal recordings:

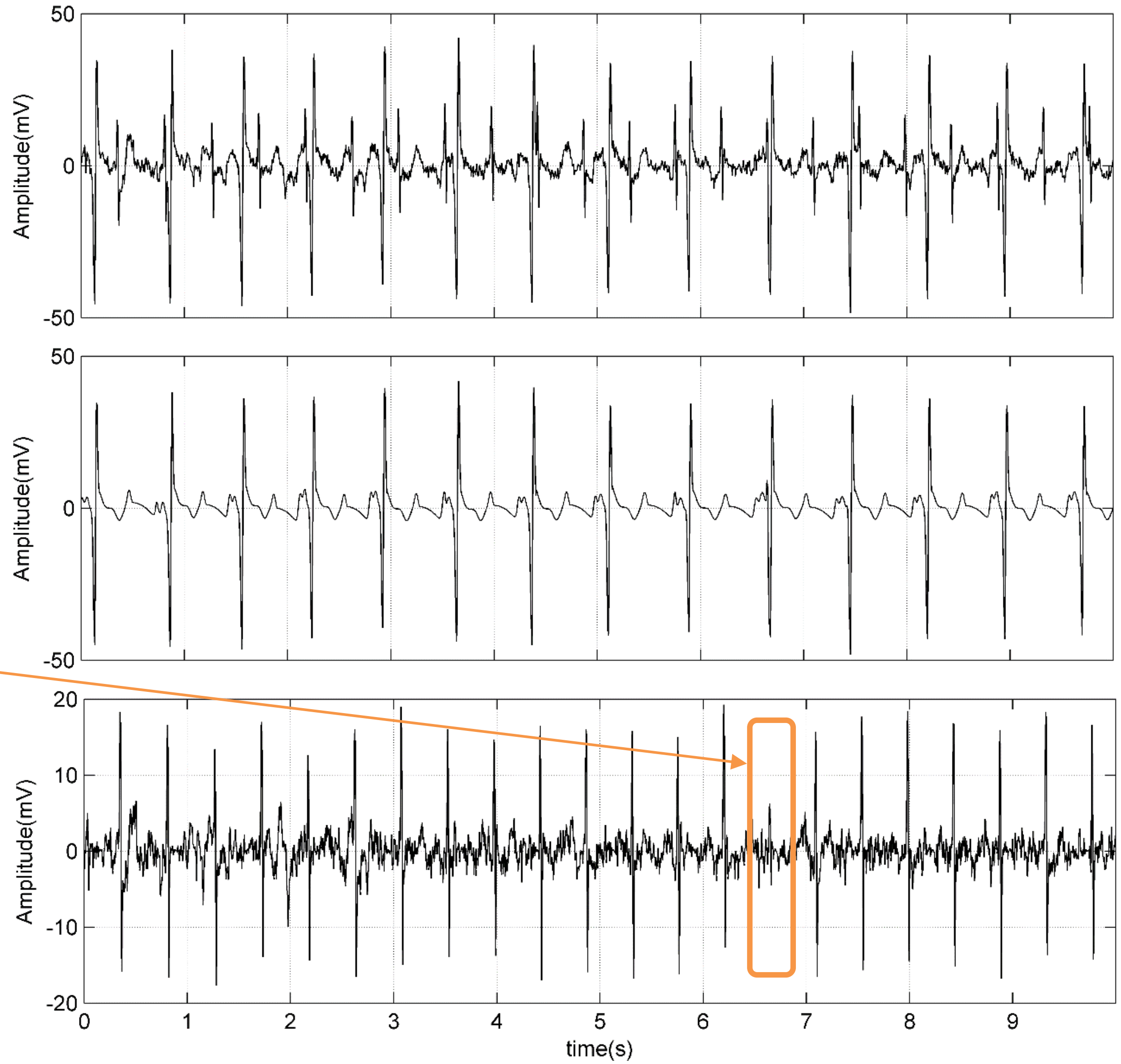


Ref: R. Sameni, M.B. Shamsollahi, and C. Jutten (2008). Model-based Bayesian filtering of cardiac contaminants from biomedical recordings. *Physiological Measurement*, *29*(5), 595.

Maternal ECG Cancellation using Kalman Filters

Example:

fECG removed due to temporal maternal and fetal QRS overlap



Original maternal abdominal signal

-

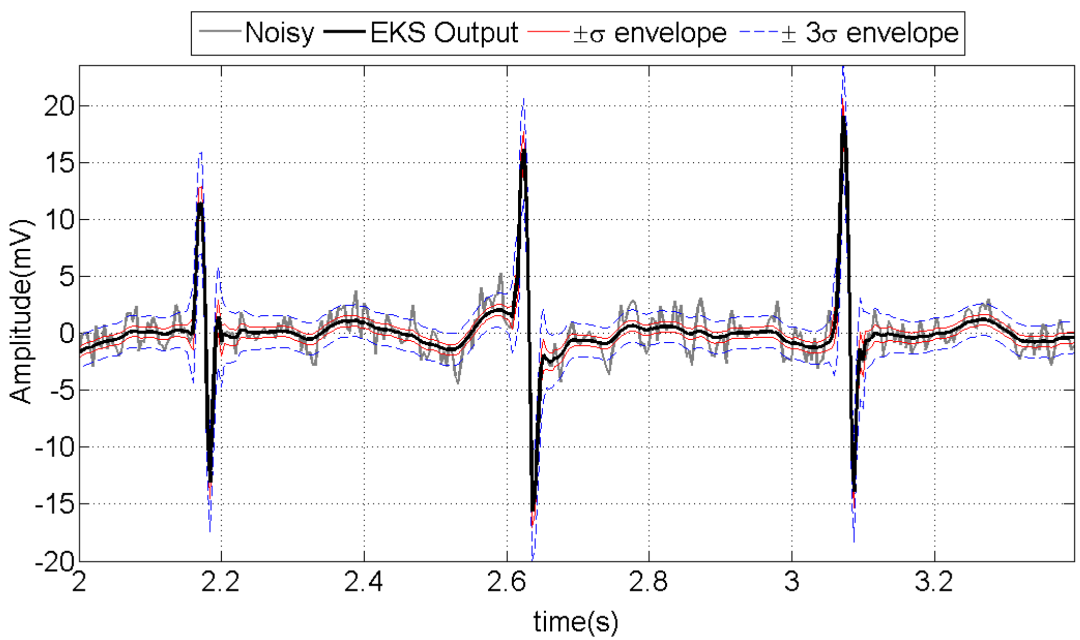
Estimated maternal ECG using Kalman filter

=

Residual fetal ECG plus noise

FECG Post-Extraction Kalman Smoothing

- The extended Kalman filter detailed before can be used for post-processing the extracted fetal ECG
- An additional benefit of the Bayesian framework is the estimation of confidence intervals for the estimated signals

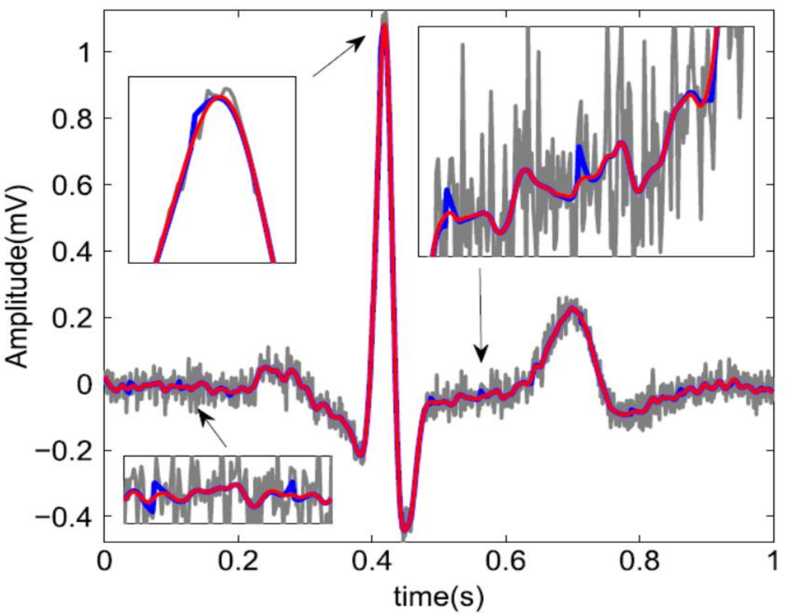


Ref: R. Sameni. "Extraction of fetal cardiac signals from an array of maternal abdominal recordings." PhD diss., Institut National Polytechnique de Grenoble-INPG; Sharif University of Technology (SUT), 2008.

ECG Denoising Using Smoothness Priors

- Another method for ECG denoising, which does not require prior dynamics is based on piece-wise smoothness priors.
- This approach is closely related to wavelet denoising, Wiener filter and Tikhonov regularization.

$$\hat{\boldsymbol{\theta}}_k = \arg\min_{\boldsymbol{\theta}_k} \|\mathbf{x}_k - \boldsymbol{\theta}_k\|^2, \ \text{s.t.} \ \|\tilde{\mathbf{D}}_d \bar{\boldsymbol{\theta}}_k\|^2 \leq \epsilon_k^2$$



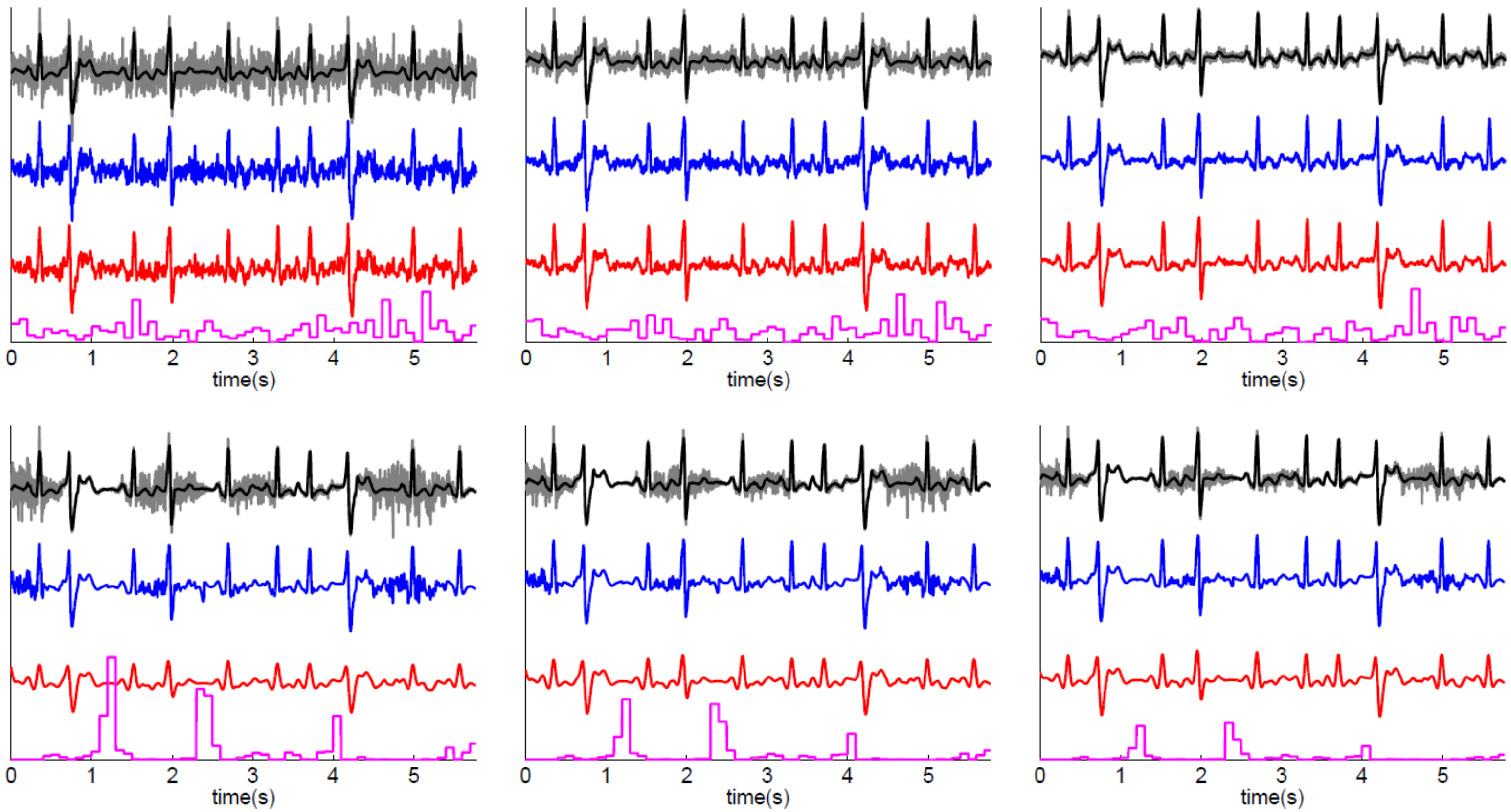
Ref: Sameni, R. (2017). Online filtering using piecewise smoothness priors: Application to normal and abnormal electrocardiogram denoising. *Signal Processing*, *133*, 52-63.

ECG Denoising Using Smoothness Priors

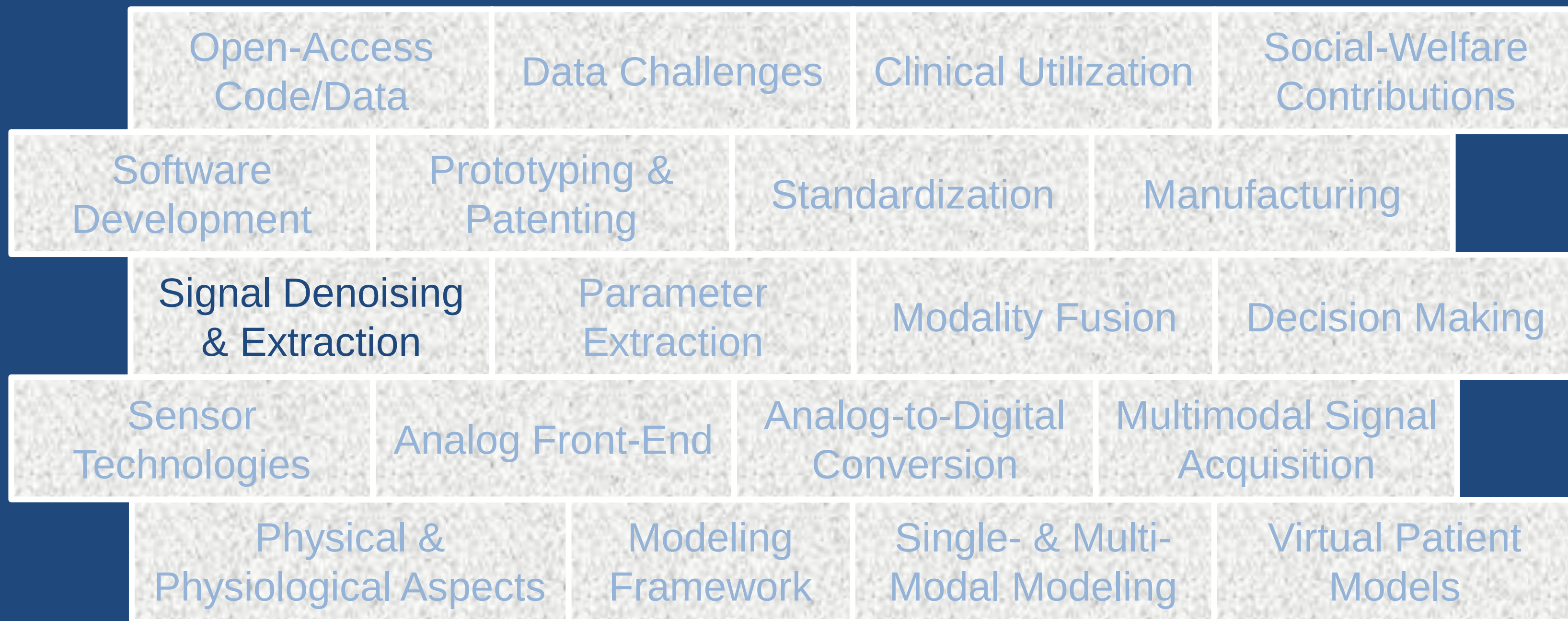
Example: Abnormal ECG contaminated by stationary/nonstationary noise

Stationary noise

Nonstationary noise



Ref: Sameni, R. (2017). Online filtering using piecewise smoothness priors: Application to normal and abnormal electrocardiogram denoising. *Signal Processing*, *133*, 52-63.

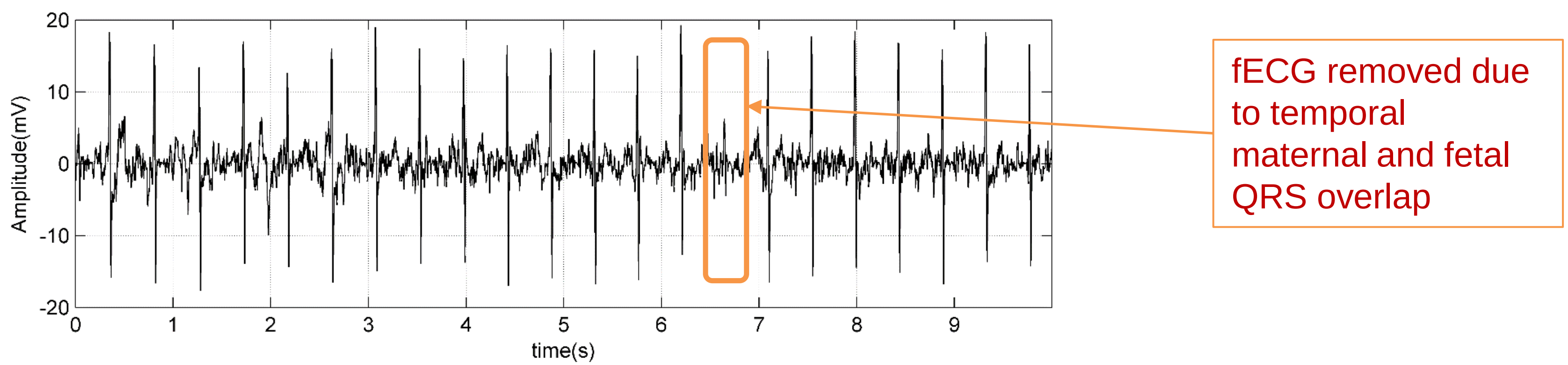


Multichannel Fetal Cardiac Signal Extraction

Maternal-Fetal QRS Overlap

- There is no synchrony between the maternal and fetal ECG ► the QRS complex of the mother frequently overlaps with the fetal QRS over time
- Single-channel Kalman filters may lose the fECG during such epochs
- Solution: Multichannel processing, with the following advantages:
  - Uses the spatial diversity of the channels to separate the fetal/maternal ECG
  - Provides a multiple perspective of the fetal heart

✓ Blind and semi-blind source separation methods are fundamental techniques in this domain



The Mainstream of fECG Extraction Techniques

Effectiveness & Popularity

1900s

Direct (visual) analysis
Only possible in high signal-to-noise ratios

Cremer, 1906; Larks, 1962

1960s **Adaptive and matched filtering**
Partially effective; require reference electrodes

Farvet, 1968, Widrow et al., 1975, Park et al., 1992, Outram et al., 1995, Shao et al., 2004, Martens et al., 2007, Sameni 2008, Behar, 2016

1990s **Linear decomposition**
Rather effective; decompose the signals onto fixed or data-driven basis functions

Li et al., 1995, Akay et al., 1996, Khamene et al., 2000

1990s **Nonlinear decomposition**
Rather effective, but empirical; require prior information

Schreiber & Kaplan, 1996a, Schreiber & Kaplan, 1996b, Richter et al., 1998, Kantz & Schreiber, 1998, Kotas, 2004

1980s **Blind & semi-blind source separation** 2019
Very effective; require multiple channels

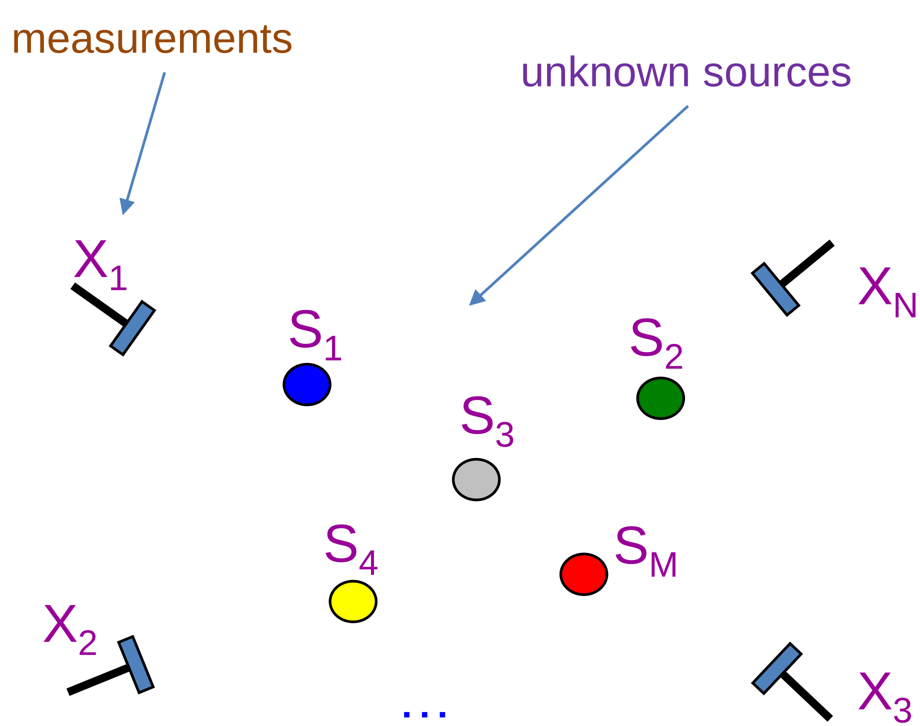
van Oosterom, 1986, Zarzoso et al., 1997, Cardoso, 1998, De Lathauwer et al., 2000, Barros & Cichocki, 2001, Zhang & Yi, 2006, Li & Yi, 2008, Vigneron et al., 2003, Jafari & Chambers, 2005, Sameni, 2008, Biglari 2016, Fatemi 2017, Jamshidian 2019

Hybrid methods have emerged

Blind Source Separation (BSS)

Data Model: The most classical case of BSS with a proven solution is for linear mixtures of independent sources (random variables or random processes).

Linear Model: $\mathbf{x}_i = \mathbf{a}_{i,1}\mathbf{s}_1 + \mathbf{a}_{i,2}\mathbf{s}_2 + \ldots + \mathbf{a}_{i,M}\mathbf{s}_M, \quad \mathbf{i} = \mathbf{1,2,\ldots,N}$



$$\begin{bmatrix} \mathbf{x}_1 \\ \mathbf{x}_2 \\ \\ \mathbf{x}_N \end{bmatrix} = \begin{bmatrix} \mathbf{a}_{11} & \mathbf{a}_{12} & & \mathbf{a}_{1M} \\ \mathbf{a}_{21} & . & & . \\ & & . & . \\ \mathbf{a}_{N1} & . & . & \mathbf{a}_{NM} \end{bmatrix} . \begin{bmatrix} \mathbf{s}_1 \\ \mathbf{s}_2 \\ \\ \mathbf{s}_M \end{bmatrix}$$

Or in matrix form: $\mathbf{X} = \mathbf{AS}$

In the noisy case: $\mathbf{X} = \mathbf{A} \cdot \mathbf{S} + \mathbf{n}$ noise

Multichannel Maternal Abdominal Signal Model

$$\mathbf{x}(\mathrm{t}) = \mathbf{H}_{\mathrm{m}}\mathbf{s}_{\mathrm{m}}(\mathrm{t}) + \mathbf{H}_{\mathrm{f}}\mathbf{s}_{\mathrm{f}}(\mathrm{t}) + \mathbf{n}(\mathrm{t})$$

- $\mathbf{x}(\mathrm{t}) \in \mathbb{R}^N$ is N channels of maternal abdominal recordings at time t
- $\mathbf{n}(\mathrm{t}) \in \mathbb{R}^N$ is the observation noise
- $\mathbf{s}_{\mathrm{m}}(\mathrm{t}) \in \mathbb{R}^M$ is the maternal ECG components with M effective dimensions
- $\mathbf{s}_{\mathrm{f}}(\mathrm{t}) \in \mathbb{R}^L$ is the fetal ECG components with L effective dimensions
- $\mathbf{H}_{\mathrm{m}} \in \mathbb{R}^{N\times M}$ and $\mathbf{H}_{\mathrm{f}} \in \mathbb{R}^{N\times L}$ are unknown linear matrices, which map the heart signals to the maternal abdomen
- $\mathbf{s}_{\mathrm{m}}(\mathrm{t})$ and $\mathbf{s}_{\mathrm{f}}(\mathrm{t})$ are statistically independent

Notes:

- The model is very accurate in stationary scenarios (when $\mathbf{H}_{\mathrm{m}}$ and $\mathbf{H}_{\mathrm{f}}$ are constant)
- In theory, due to the spatial distributed-ness of the cardiac source signals, M and L tend to infinity. However in practice, using far-field approximations, the effective number of dimensions are $M = 5 \dots 6$ and $L = 2 \dots 3$.

Ref: Jamshidian-Tehrani, Fahimeh, and Reza Sameni. "Fetal ECG extraction from time-varying and low-rank noninvasive maternal abdominal recordings." *Physiological measurement* 39.12 (2018): 125008.

A Blind-Source Separation Formulation

- The data model can be rewritten in terms of a BSS problem:

$$\mathbf{x}(\mathrm{t}) = [\mathbf{H}_\mathbf{m} \quad | \quad \mathbf{H}_\mathrm{f}] \begin{bmatrix} \mathbf{s}_\mathrm{m}(\mathrm{t}) \\ - \\ \mathbf{s}_\mathrm{f}(\mathrm{t}) \end{bmatrix} + \mathbf{n}(\mathrm{t})$$
$$= \mathbf{H}\mathbf{s}(\mathrm{t}) + \mathbf{n}(\mathrm{t})$$

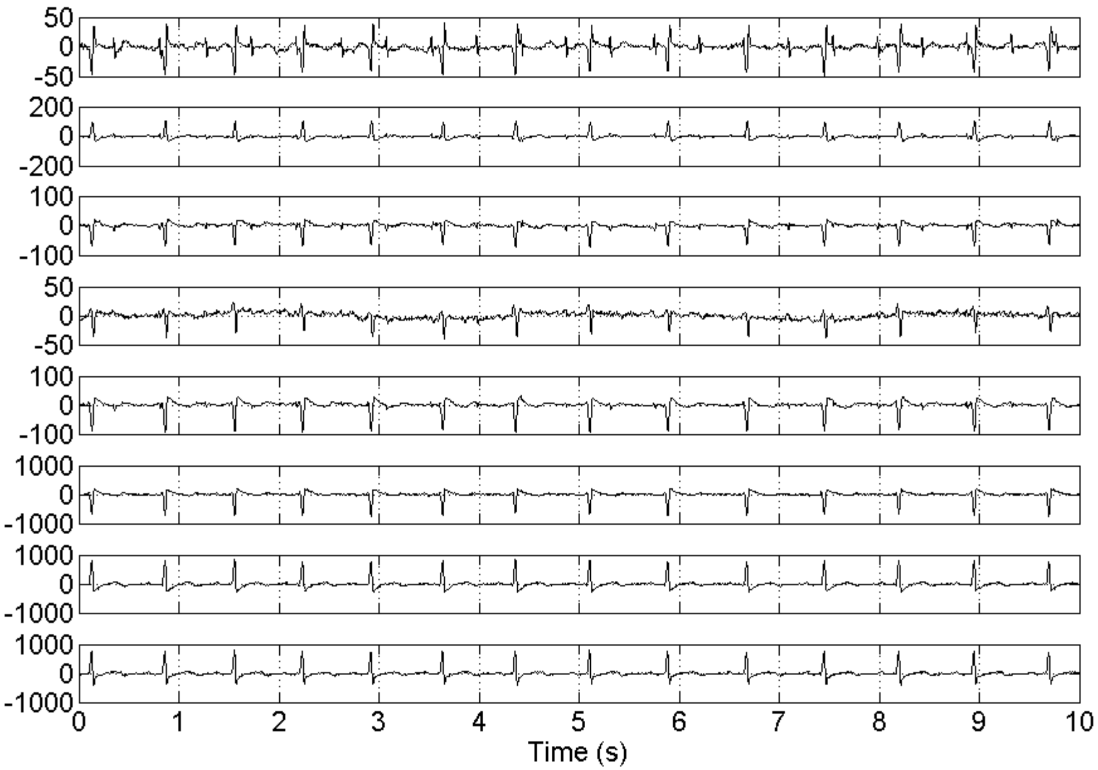
- If the abdominal channels are well-spread across the maternal abdomen (to avoid singular mixtures), and if $M + L \leq N$ (more recordings than effective dimensions), the BSS problem has a solution.
- So, ICA can be used to separate the maternal and fetal ECG signals
- With a good electrode placement, even classical ICA methods are rather successful in fECG extraction

✓ *That's why fECG extraction has been one of the favorite problems for BSS experts!*

Further reading on ISA: J.-F. Cardoso, "Multidimensional independent component analysis," in Proceedings of the IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP '98), vol. 4, May 1998, pp. 1941– 1944.

Naïve ICA for Fetal ECG Extraction

- Example: The DaISy fECG dataset



Refer to:

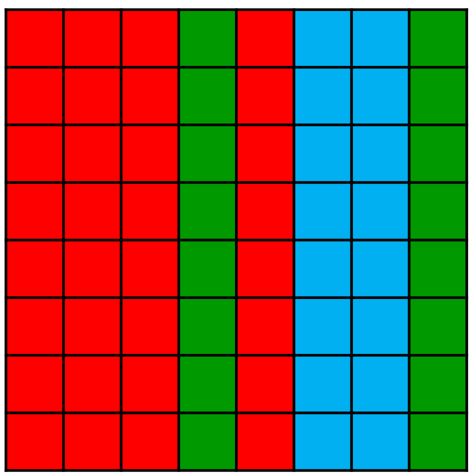
- L. De Lathauwer, B. De Moor, and J. Vandewalle, Fetal electrocardiogram extraction by blind source subspace separation," IEEE Trans. Biomed. Eng., vol. 47, pp. 567-572, May 2000.
- Zarzoso, V., & Nandi, A. K. (2001). Noninvasive fetal electrocardiogram extraction: blind separation versus adaptive noise cancellation. IEEE Transactions on biomedical engineering, 48(1), 12-18.

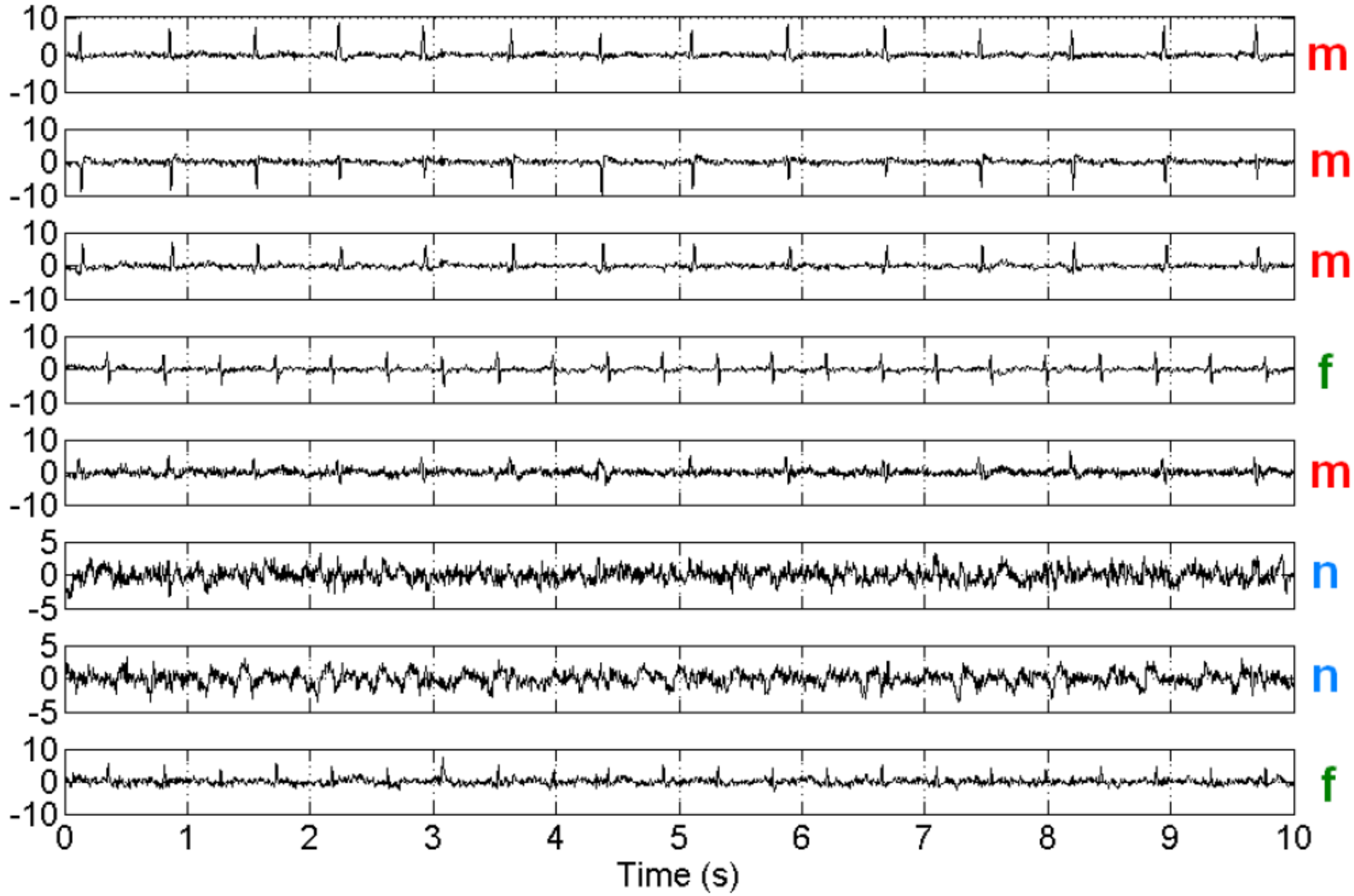
Naïve ICA for Fetal ECG Extraction (continued)

Independent components extracted by the JADE algorithm

$$\boldsymbol{x}(t) = \boldsymbol{A}\boldsymbol{s}(t) + \boldsymbol{n}(t)$$

Mixing matrix (**A**)
maternal/fetal/noise subspace partitioning





Note: Quite similar results are obtained from other ICA methods such as FastICA, SOBI, TDSEP, etc. on this dataset.

Issues of Classical ICA for fECG Extraction

- Intrinsic limitations of ICA:
  - Source orders can not be determined
  - Source amplitude and sign can not be recovered
- Classical ICA assumptions do not exactly hold:
  - Number of sources and sensors are not equal
  - The mixtures can become singular due to electrode placement or fetal position
  - The mixture is always noisy; no guarantee for source extraction
  - Time-varying mixtures, due to fetal motion

✓Special source separation techniques have been proposed in the literature to resolve these issues

Semi-Blind Source Separation

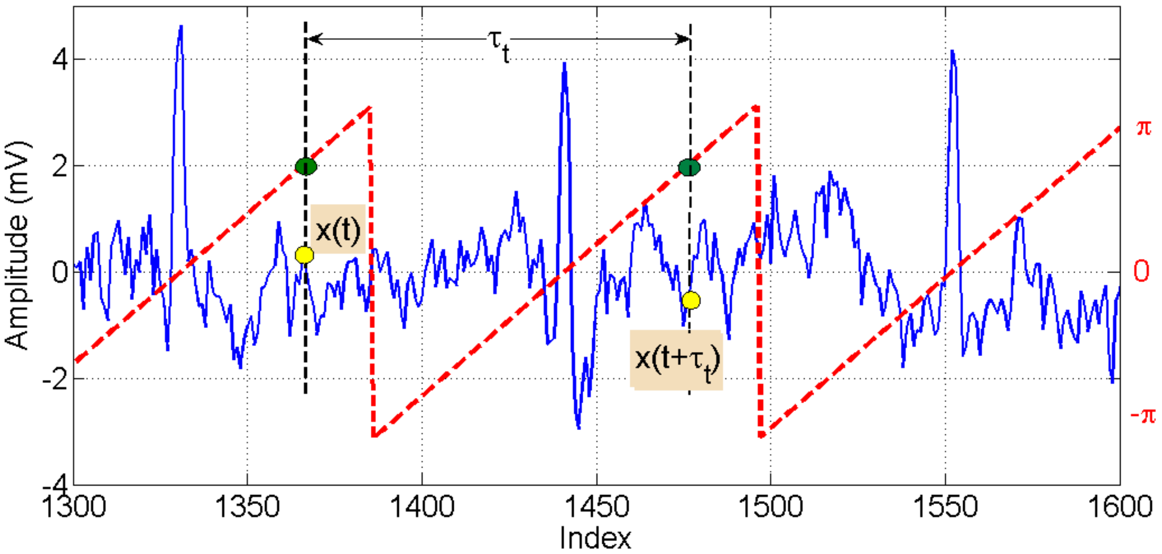
- Using problem-specific priors can be used to tailor BSS for fECG extraction ► semi-blind source separation

- Prior assumptions regarding fetal/maternal ECG mixtures:
  1. Pseudo-periodicity of the maternal and fetal ECG
  2. Synchrony of the multichannel R-peaks
  3. Inter-group independence and intra-group dependence between the maternal and fetal ECG components

Periodic Component Analysis (πCA) Algorithm

The ΠCA algorithm for ECG extraction:

1. Detect the R-peaks of the ECG of interest (a priori information)
2. Calculate the ECG phase signal θ(t)
3. Calculate the time-varying lag: $\tau_t = \mathrm{argmin}\{\tau |\ \theta(t+\tau) = \theta(t), \tau > 0\}$
4. Calculate $\mathbf{C}_x = Et\{\mathbf{x}(t)\mathbf{x}(t)^T\}$ and $\hat{\mathbf{C}}_x = E_t\{\mathbf{x}(t+\tau_t)\mathbf{x}(t)^T\}$
5. Symmetrize the lagged covariance matrix $\hat{\mathbf{C}}_x \leftarrow [\hat{\mathbf{C}}_x + \hat{\mathbf{C}}_x^T]/2$
6. Find $\mathbf{B} = \mathrm{GEVD}(\mathbf{C}_x, \hat{\mathbf{C}}_x)$
7. Calculate $\mathbf{y}(t) = \mathbf{B}\mathbf{x}(t)$

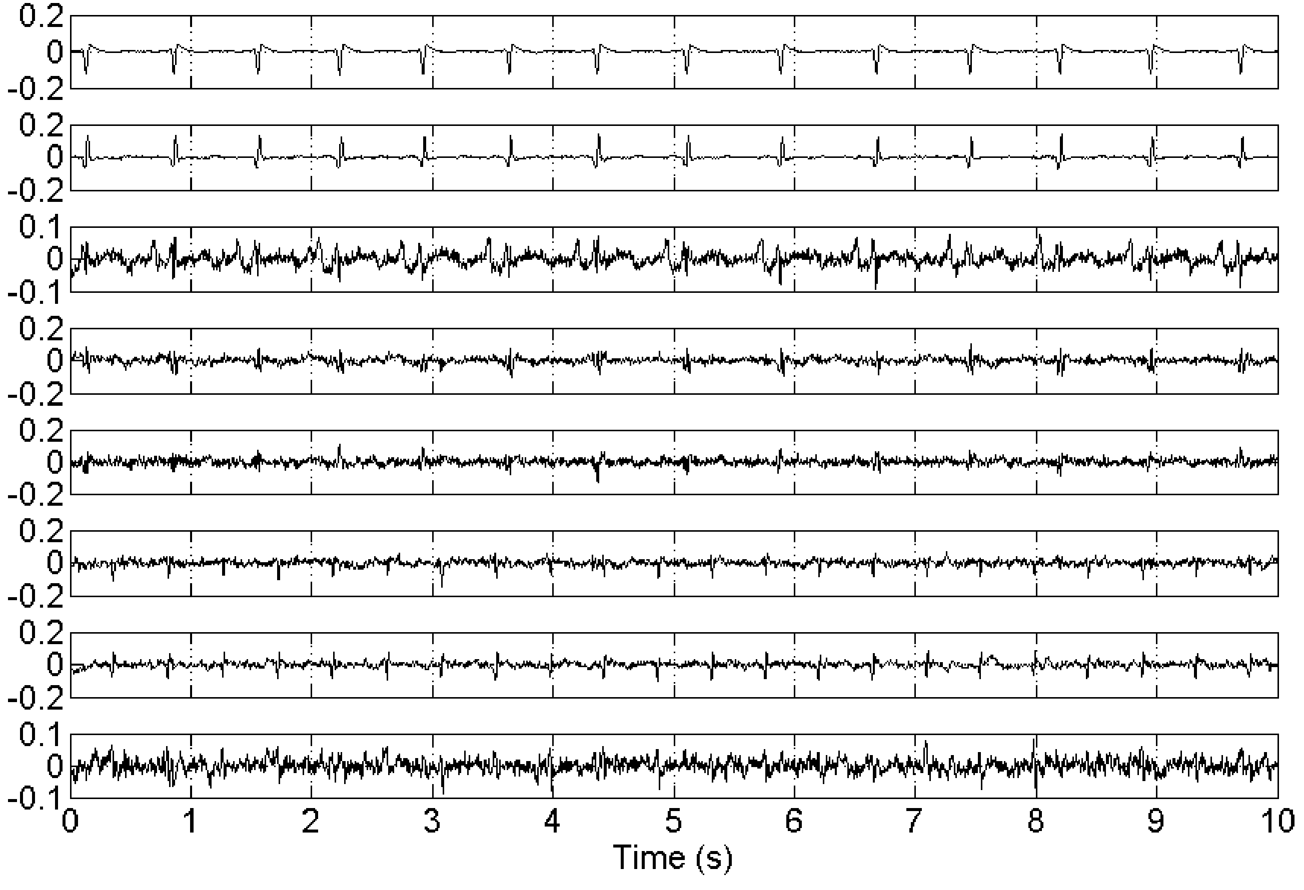


Ref:

- L. K. Saul and J. B. Allen, Periodic component analysis: An eigenvalue method for representing periodic structure in speech." in NIPS, 2000, pp. 807-813
- R. Sameni, C. Jutten, MB Shamsollahi (2008). Multichannel electrocardiogram decomposition using periodic component analysis. IEEE Transactions on Biomedical Engineering, 55(8), 1935-1940.

Periodic Component Analysis (πCA)

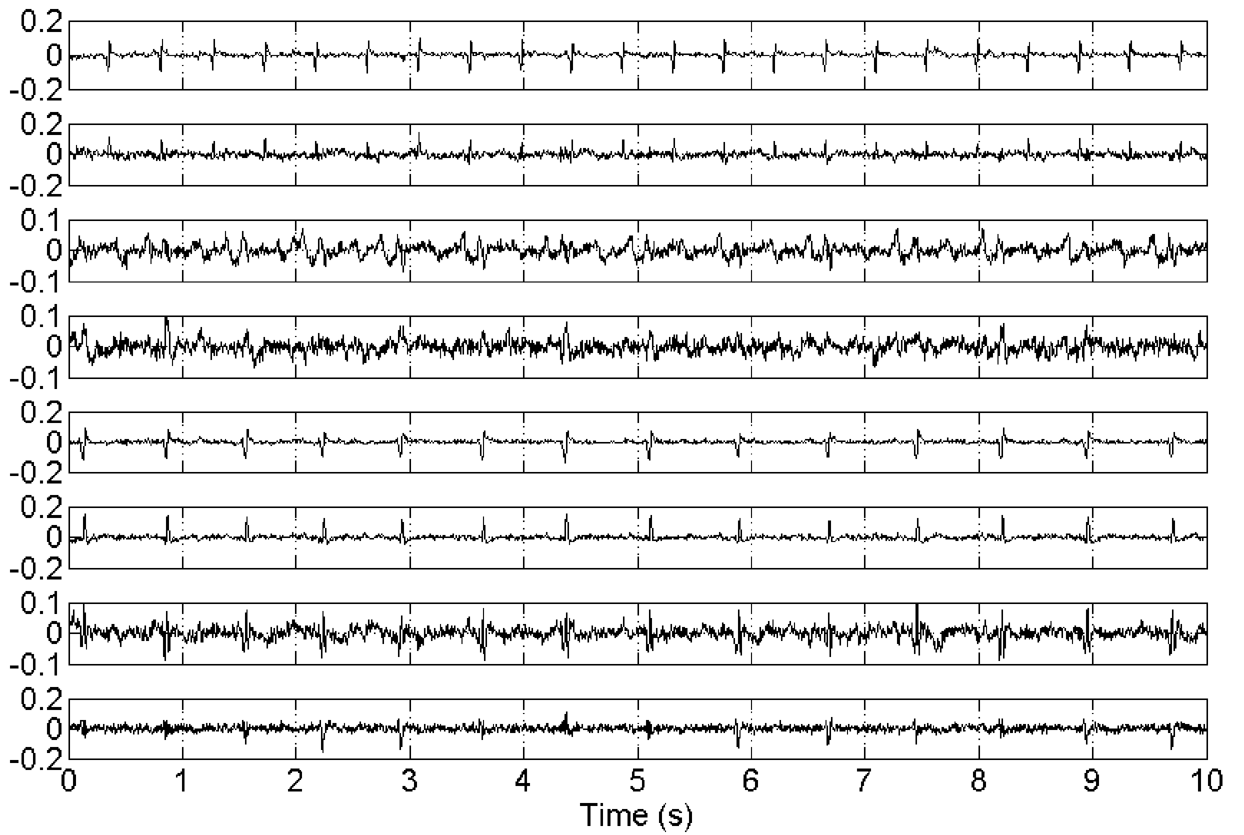
Example: πCA using maternal R-peaks



Property: sorted according to similarity with maternal ECG from top to bottom

Periodic Component Analysis (πCA)

Example: πCA using fetal R-peaks (from scalp leads or after an initial ICA or maternal-based πCA stage)



Property: sorted according to similarity with fetal ECG from top to bottom

Noisy and Singular Measurements

- Looking back at the data model $x(t)=Hs(t)+n(t)$, we have:

$$y(t)=Bx(t)= BHs(t)+Bn(t)$$

- So $y(t)$ is only an exact estimate of $s(t)$, when:

1. B is the inverse of H; no solutions when H is singular!
2. $Bn(t)=0$ ($n(t)$ is in the null-space of B); otherwise the noise remains (or is even magnified) and the estimation of B is biased

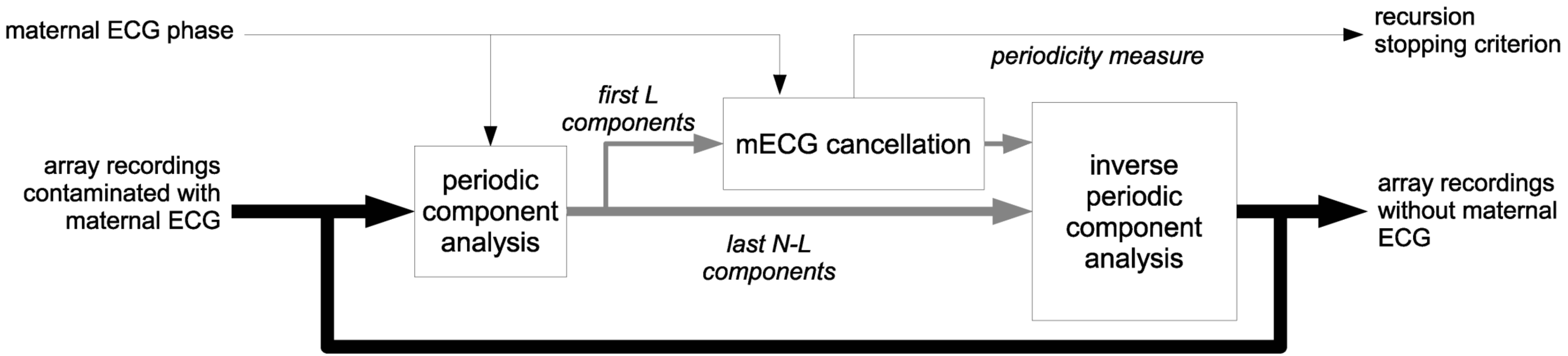
Solutions:

- Breaking the linearity of the transform!
- Denoising before source separation

The two issues can be considered in a single algorithm, which performs source separation and denoising in a deflation-wise (step-by-step) manner.

A Deflation Procedure for fECG Extraction

- The following iterative procedure can solve the problem of mixture singularity and noisy measurements at the same time:



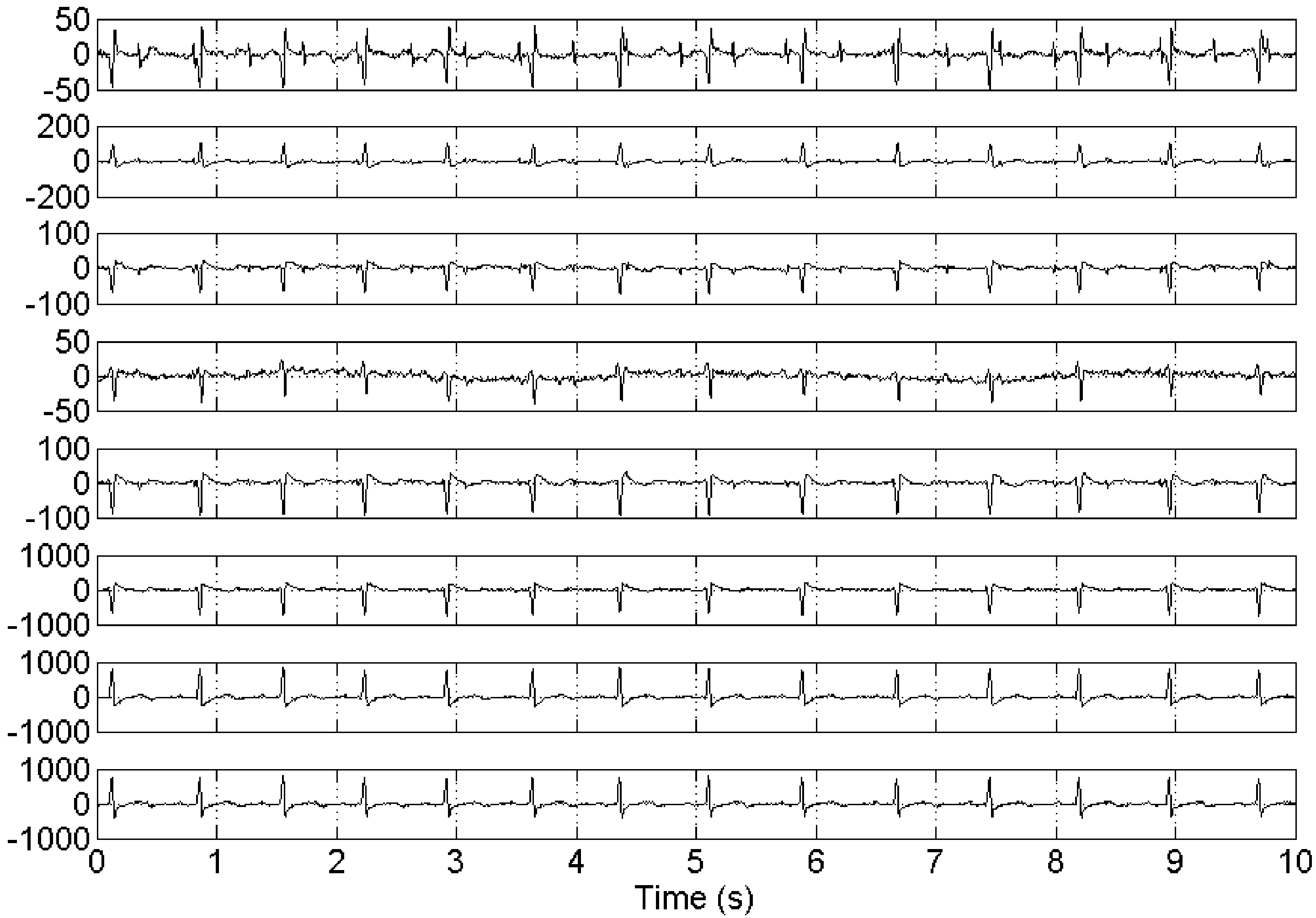
Refs:

- R. Sameni, C. Jutten, MB Shamsollahi (2010). A deflation procedure for subspace decomposition. *IEEE Transactions on Signal Processing*, *58*(4), 2363-2374.
- R. Sameni, C. Jutten, M. Shamsollahi, and G. Clifford, “Extraction of Fetal Cardiac Signals,” U.S. Patent US 2010/0137727 A1, June 3, 2010.

A Deflation Procedure for fECG Extraction

(continued)

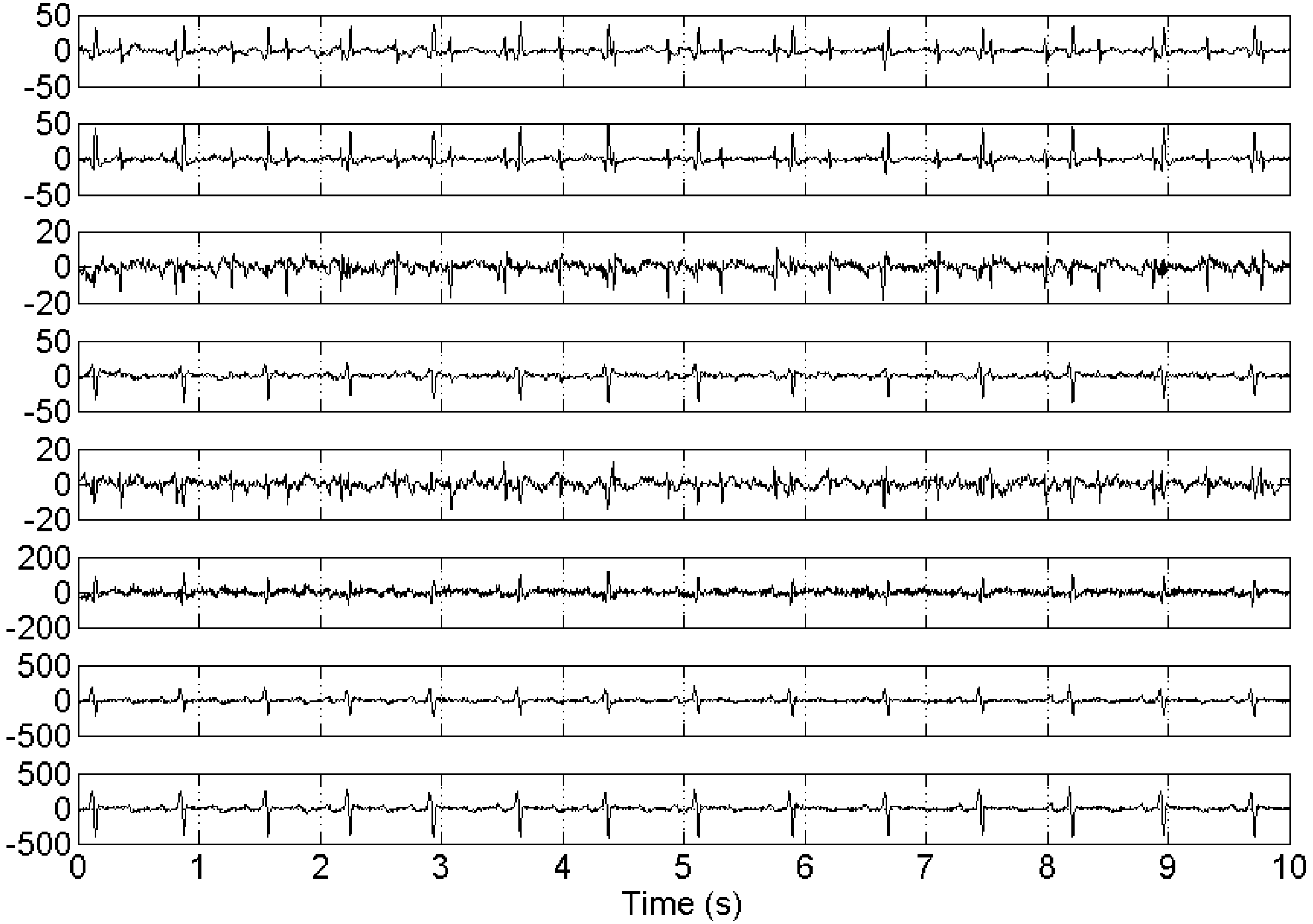
Example 1: Original signal



A Deflation Procedure for fECG Extraction

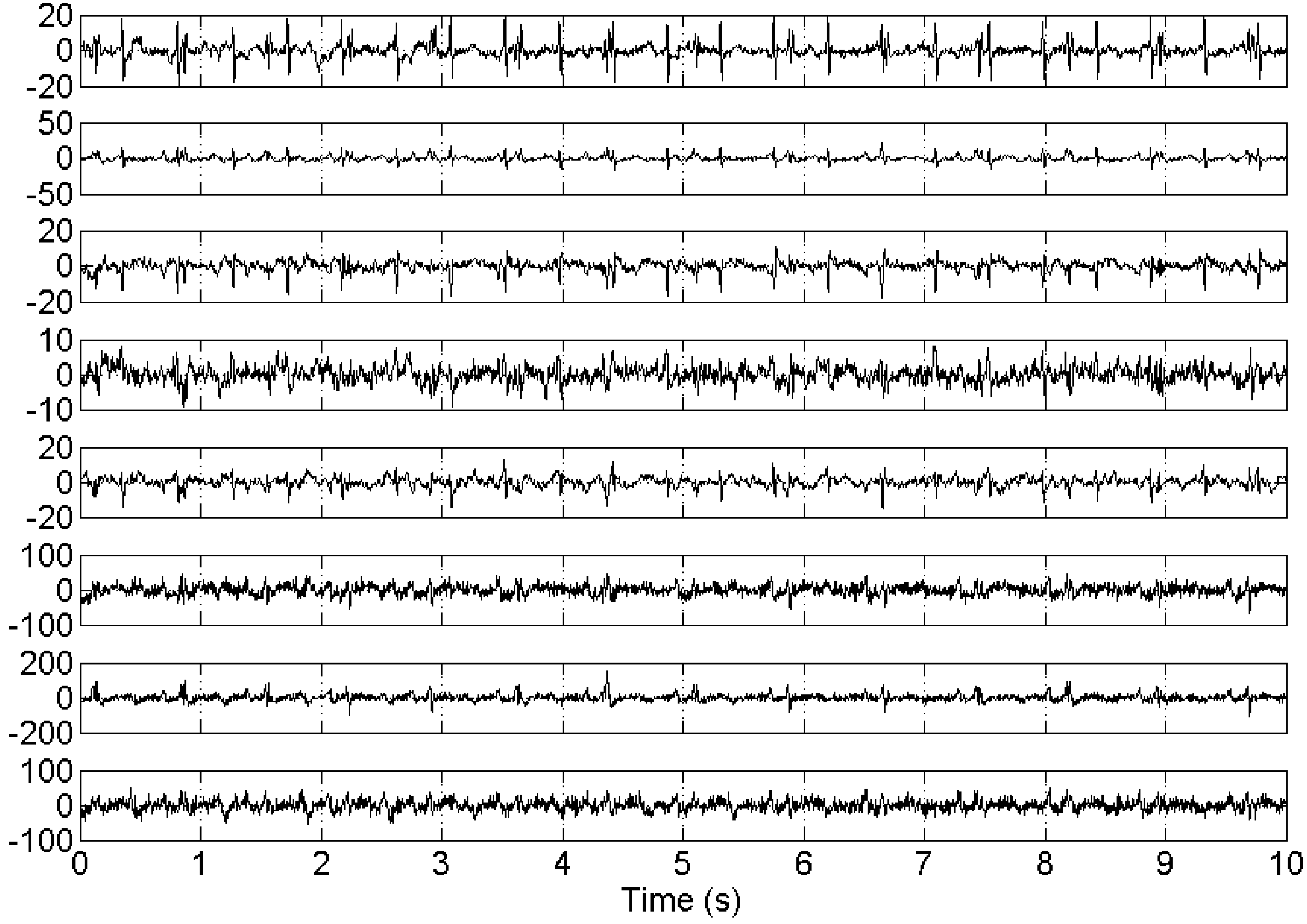
(continued)

Example 1: After 1st iteration



A Deflation Procedure for fECG Extraction
(continued)

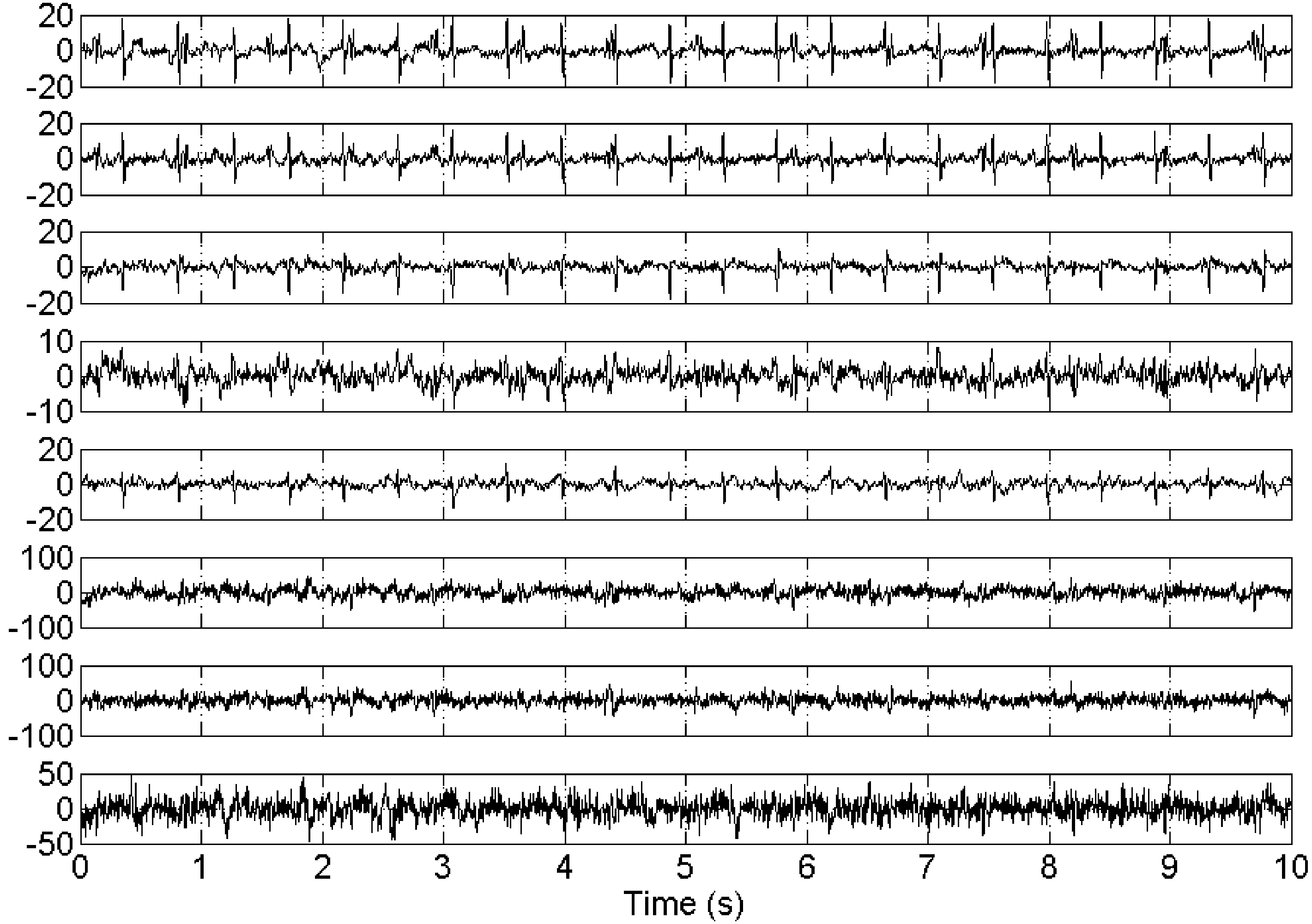
Example 1: After 2nd iteration



A Deflation Procedure for fECG Extraction

(continued)

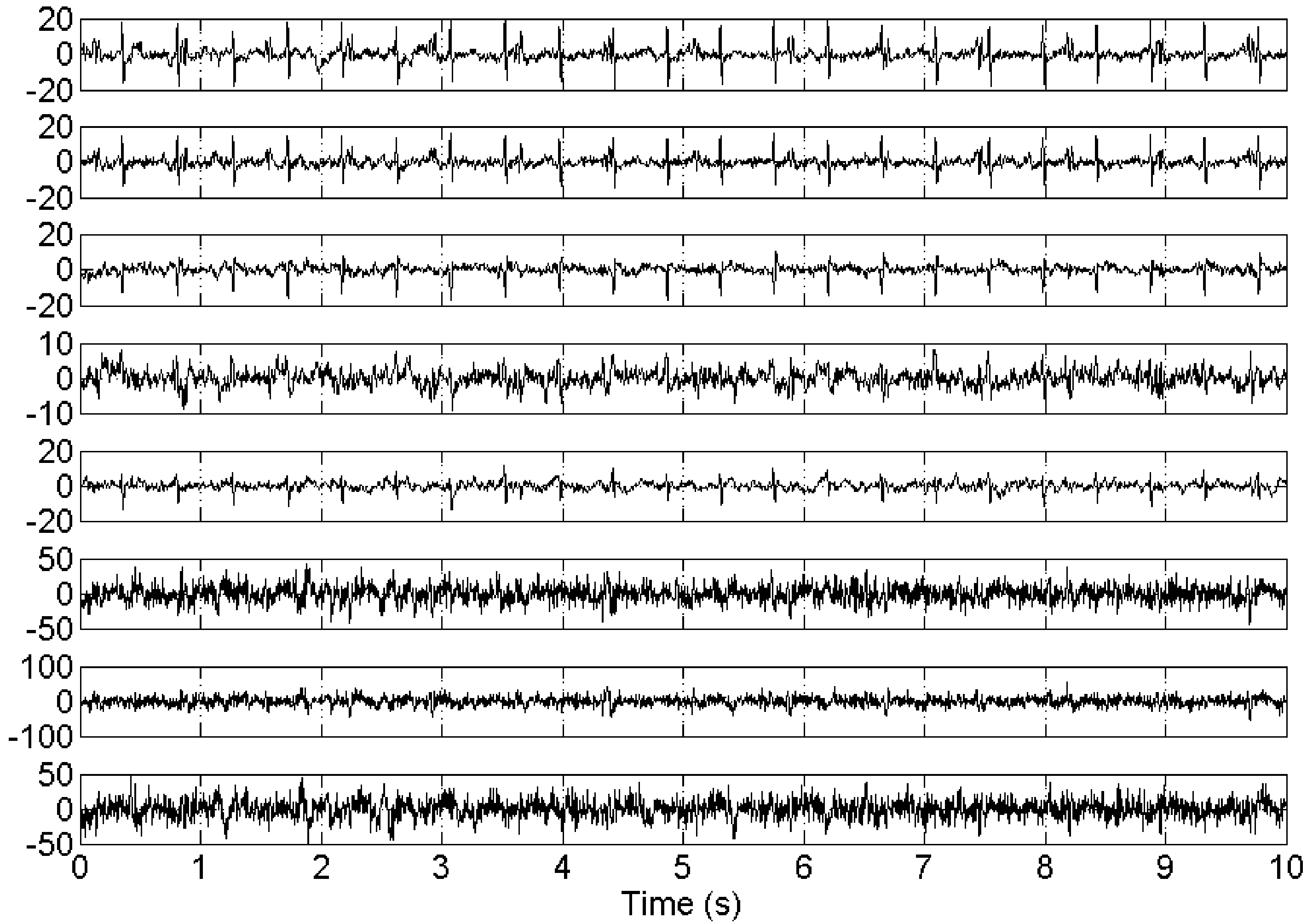
Example 1: After 3rd iteration



A Deflation Procedure for fECG Extraction

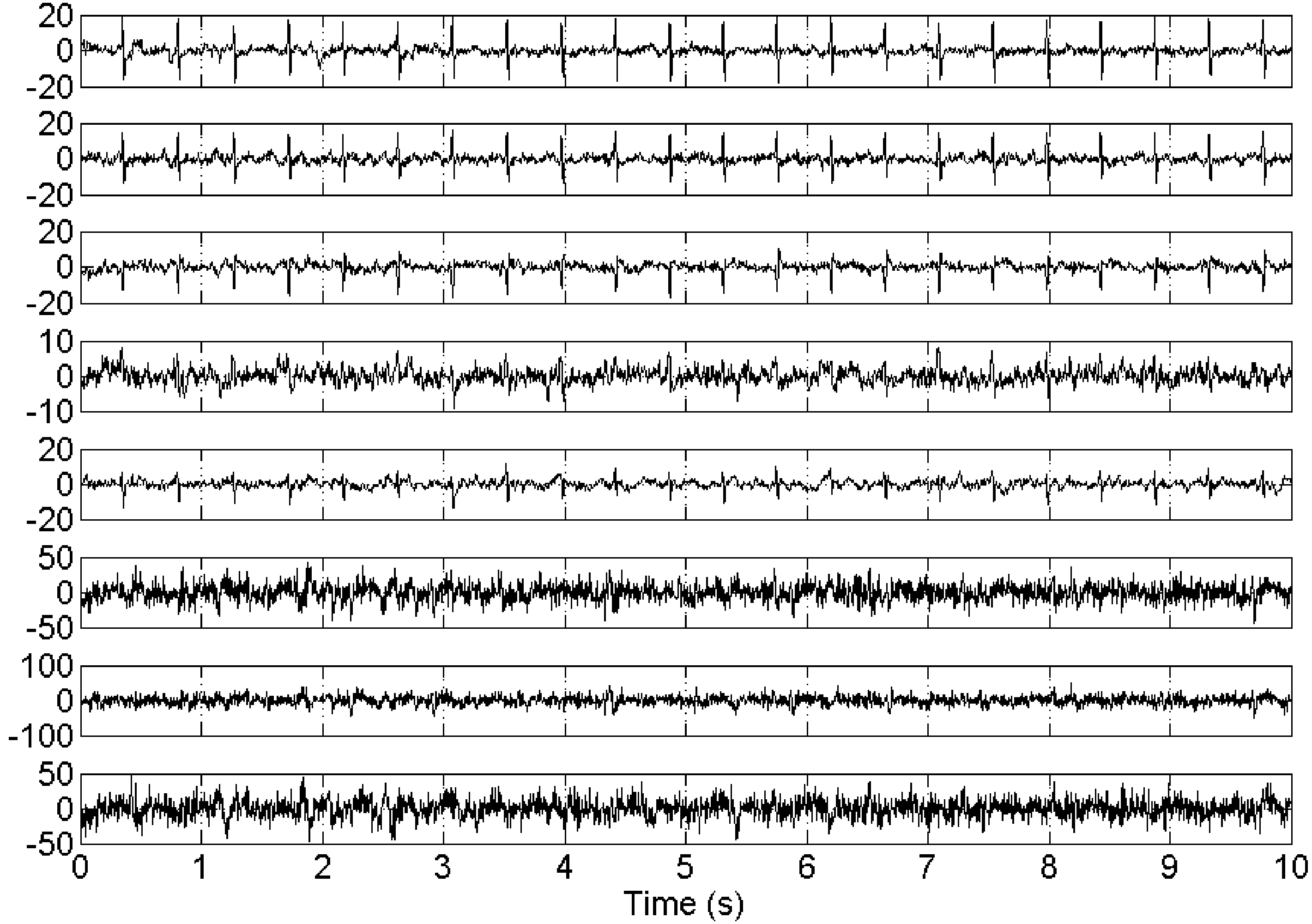
(continued)

Example 1: After 4th iteration



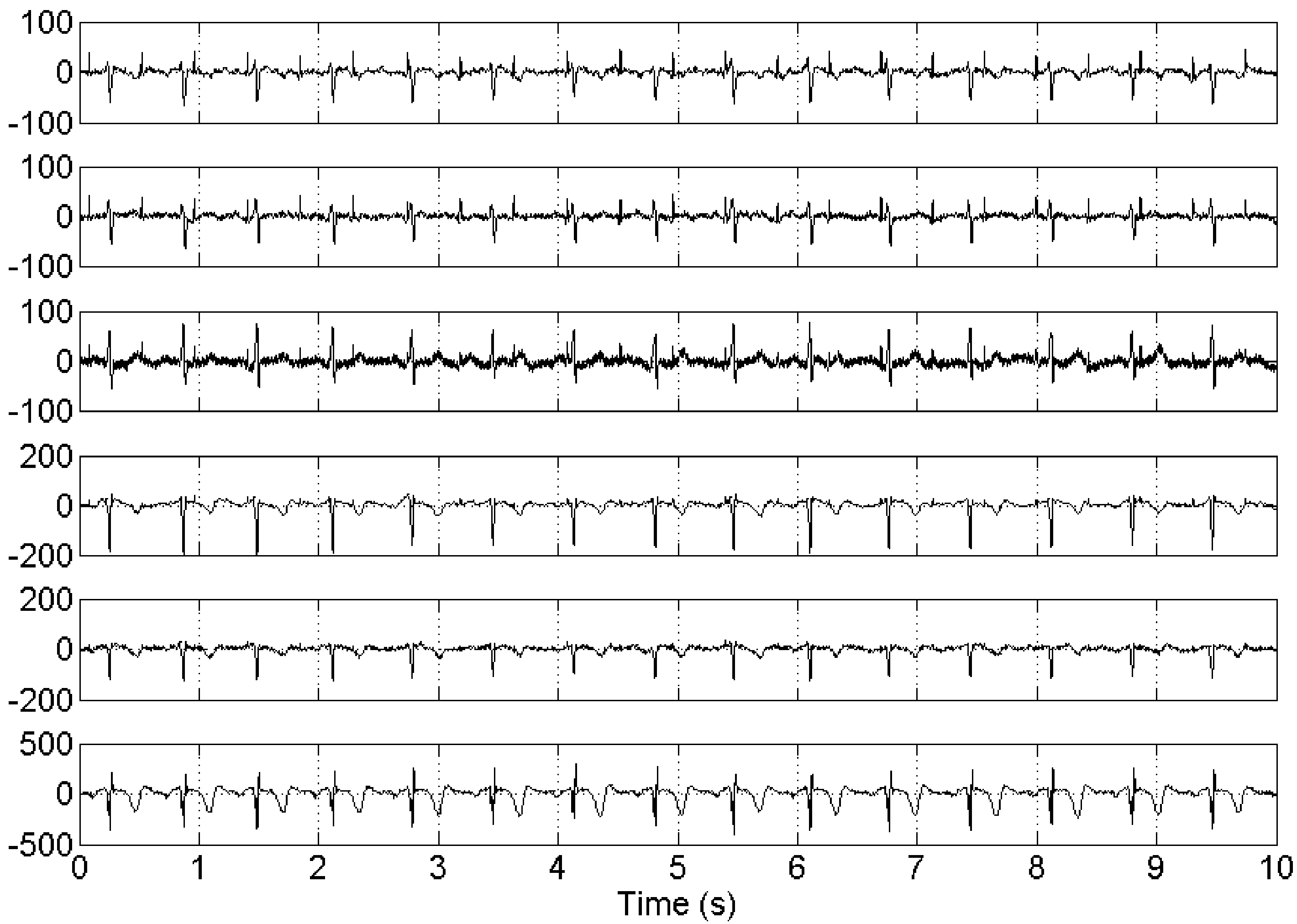
A Deflation Procedure for fECG Extraction
(continued)

Example 1: After 5th iteration (maternal ECG fully removed)



A Deflation Procedure for fECG Extraction
(continued)

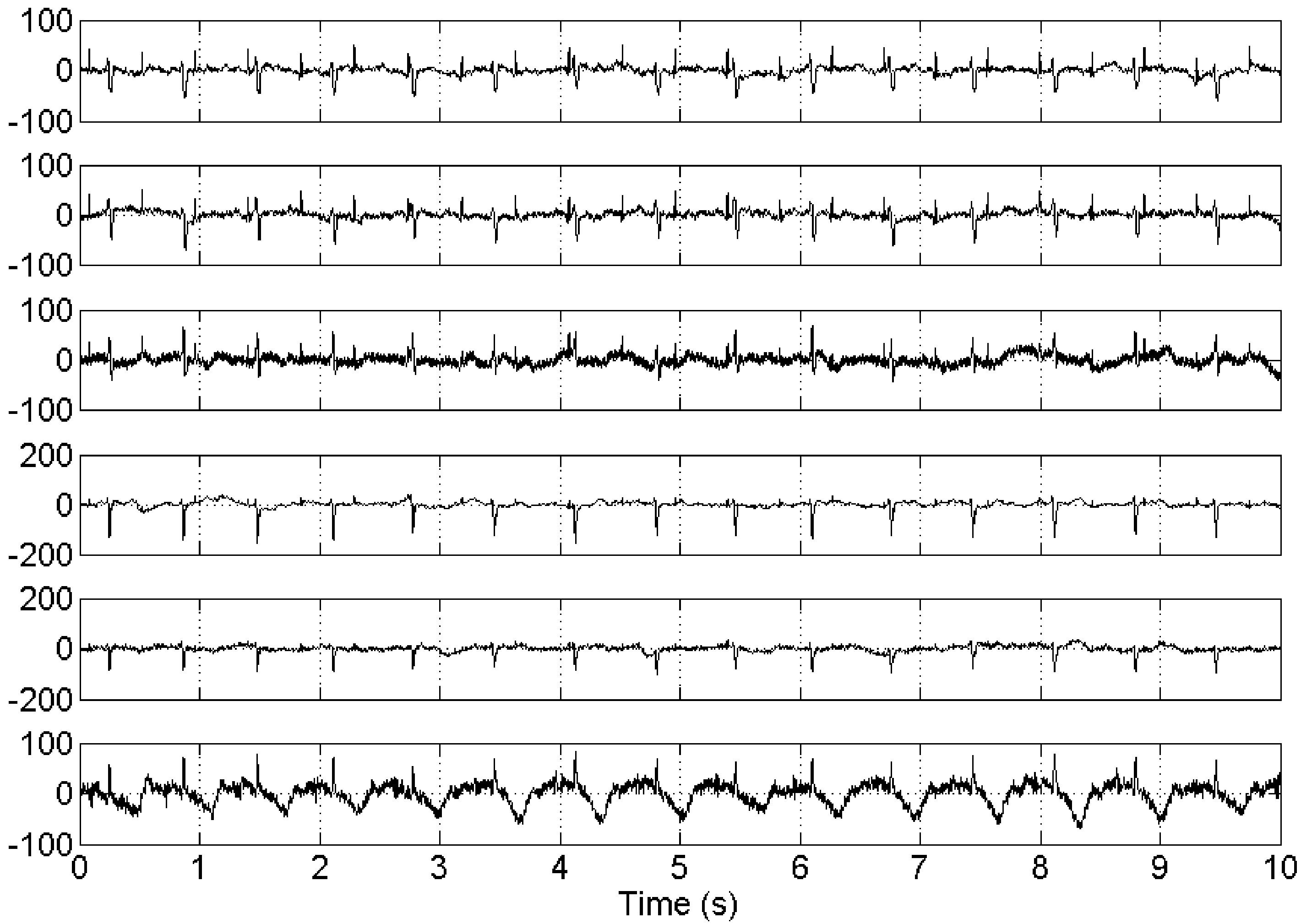
Example 2: A singular mixture (conventional ICA failed on this data)



A Deflation Procedure for fECG Extraction

(continued)

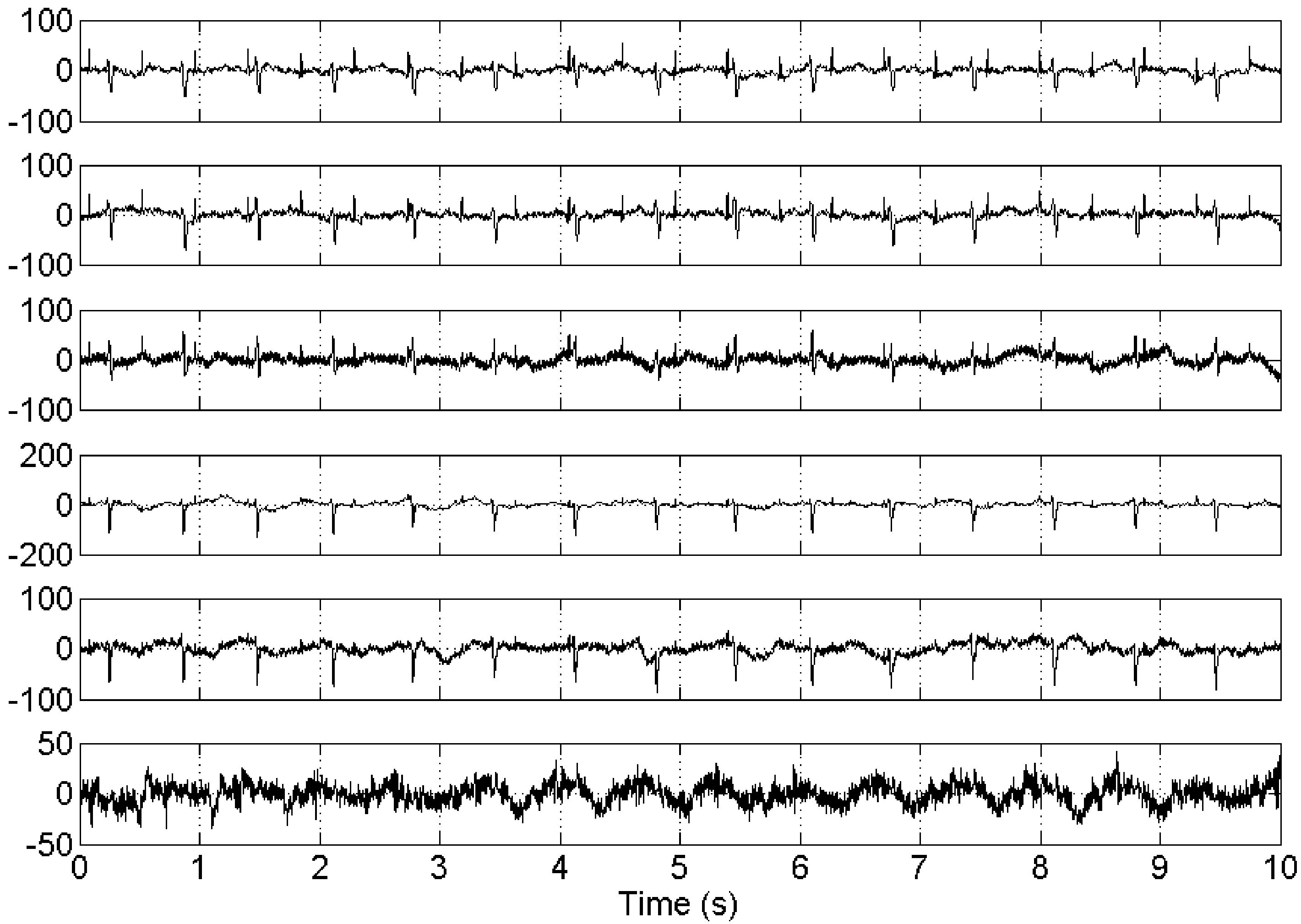
Example 2: After 1st iteration



A Deflation Procedure for fECG Extraction

(continued)

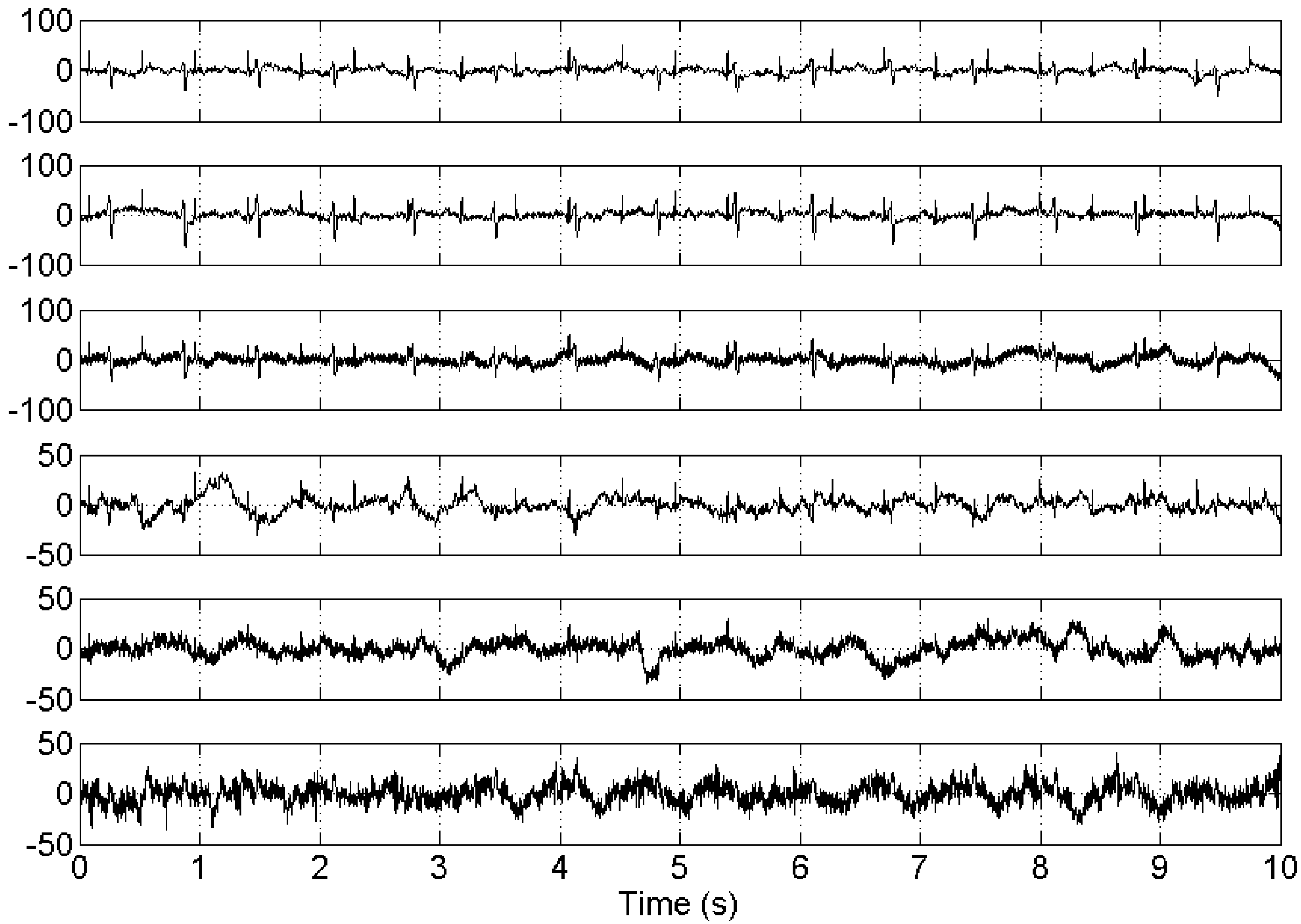
Example 2: After 2nd iteration



A Deflation Procedure for fECG Extraction

(continued)

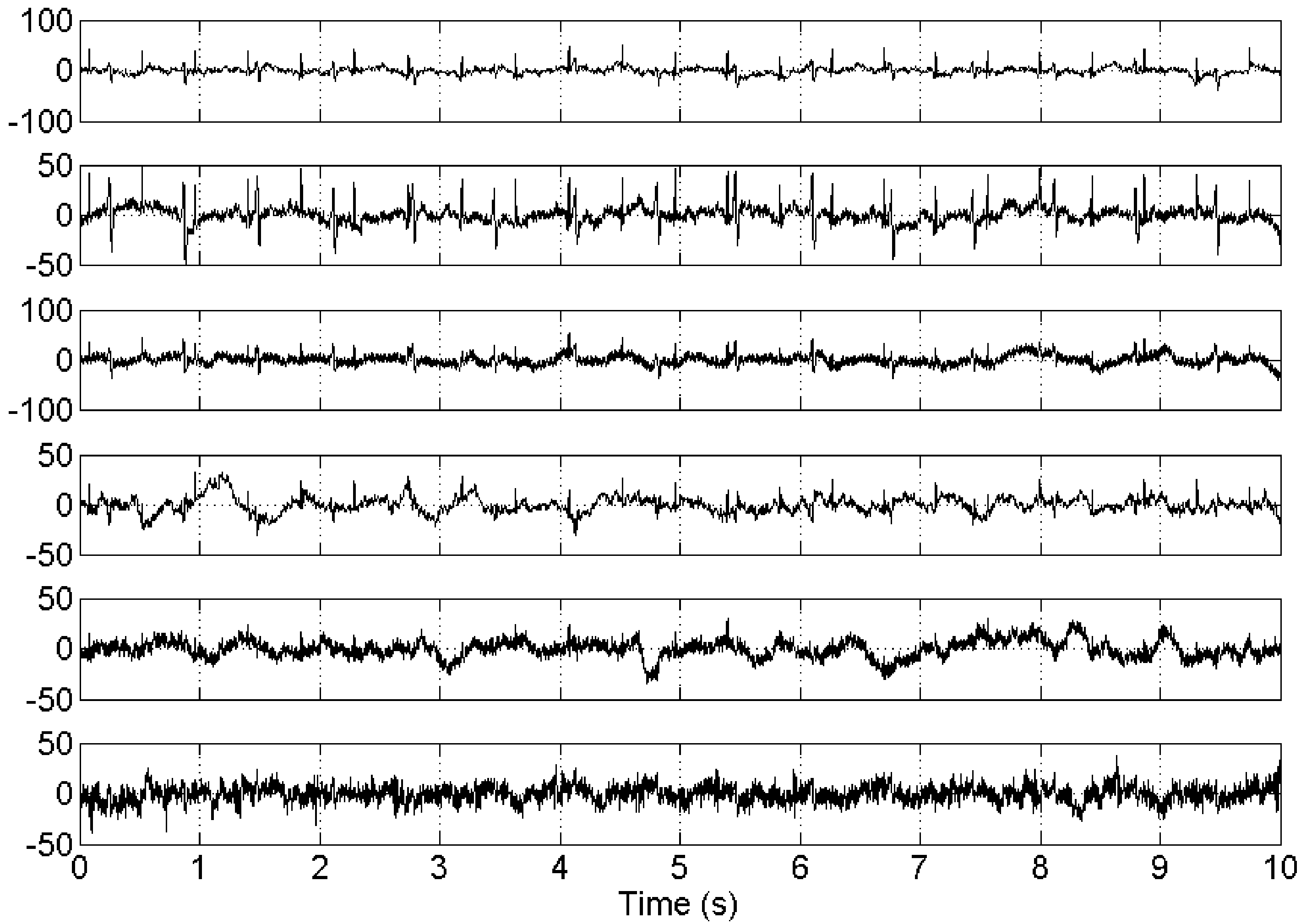
Example 2: After 3rd iteration



A Deflation Procedure for fECG Extraction

(continued)

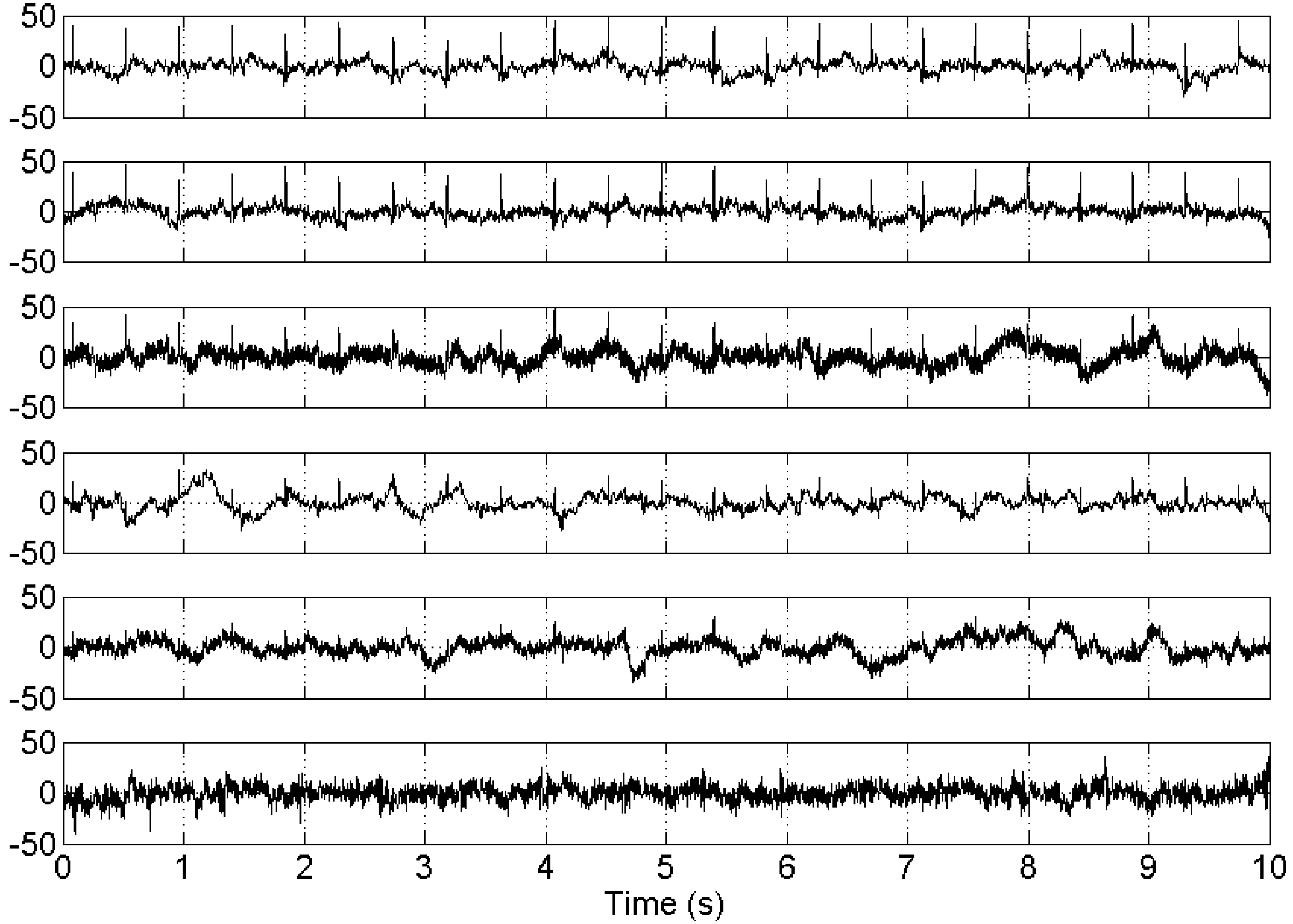
Example 2: After 4th iteration



A Deflation Procedure for fECG Extraction

(continued)

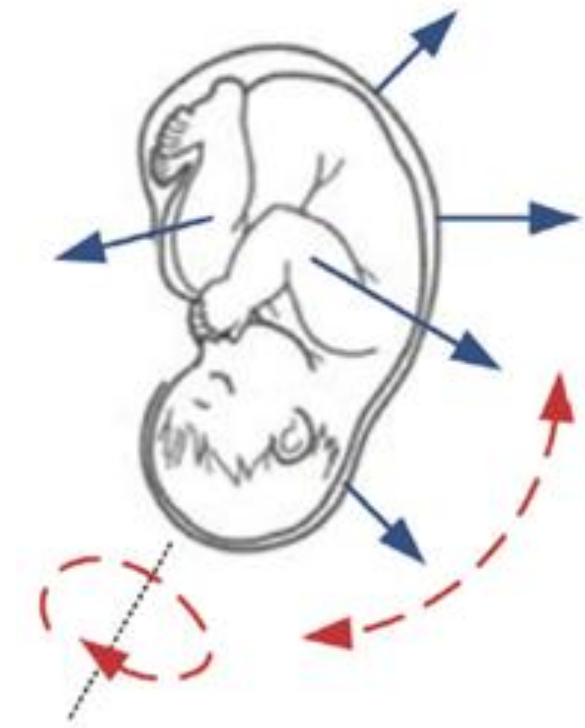
Example 2: After 5th iteration (maternal ECG fully removed)



Time-Variant Scenarios

- Time-variant mixtures are another challenge
- Due to fetal movements, temporal variations are unavoidable in long recordings
- In this case, the noiseless data model is: $x(t)=H(t)s(t)$

  Hence: $y(t)=Bx(t)=BH(t)s(t)\neq s(t)$

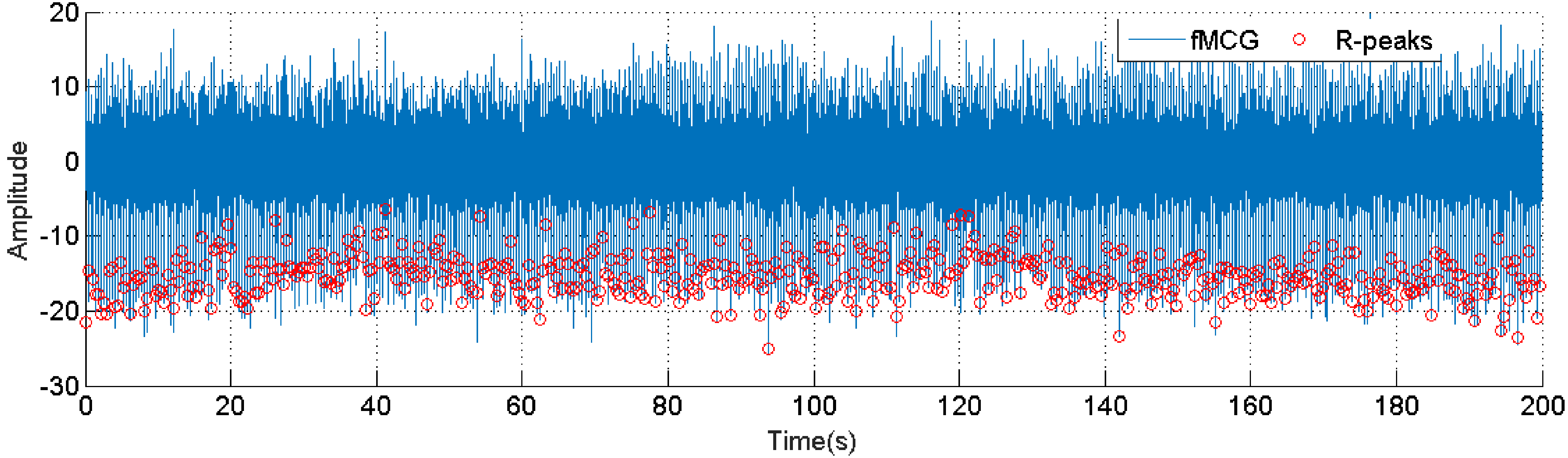


- Applying ICA, πCA, or other time-invariant algorithms to such data results in:

1. Partial separation of the sources
2. Time-varying sources which move from of channel to another

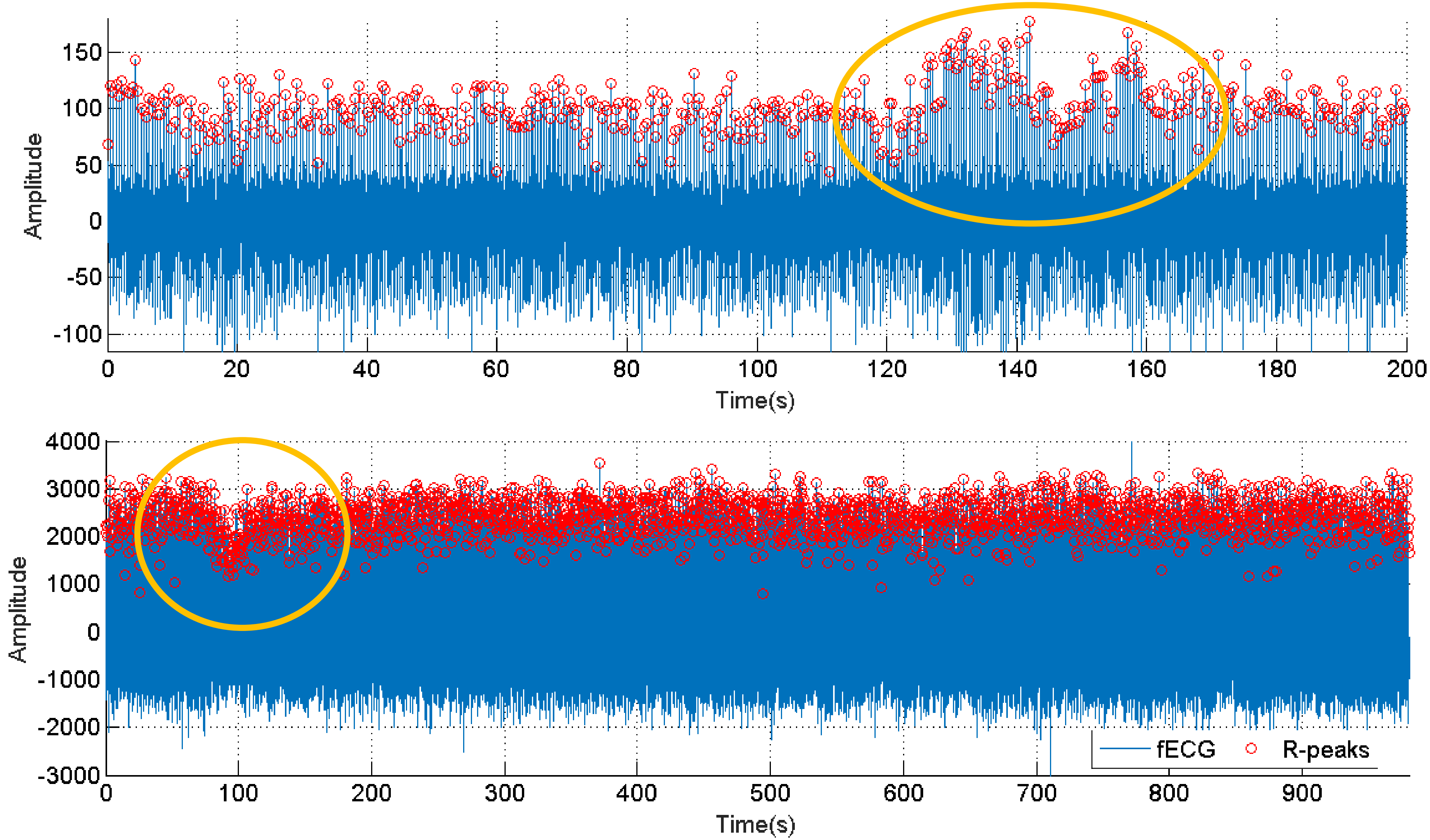
Time-Variant Scenarios

Example 1: Stationary case (for fetal MCG); no significant fetal motion observed



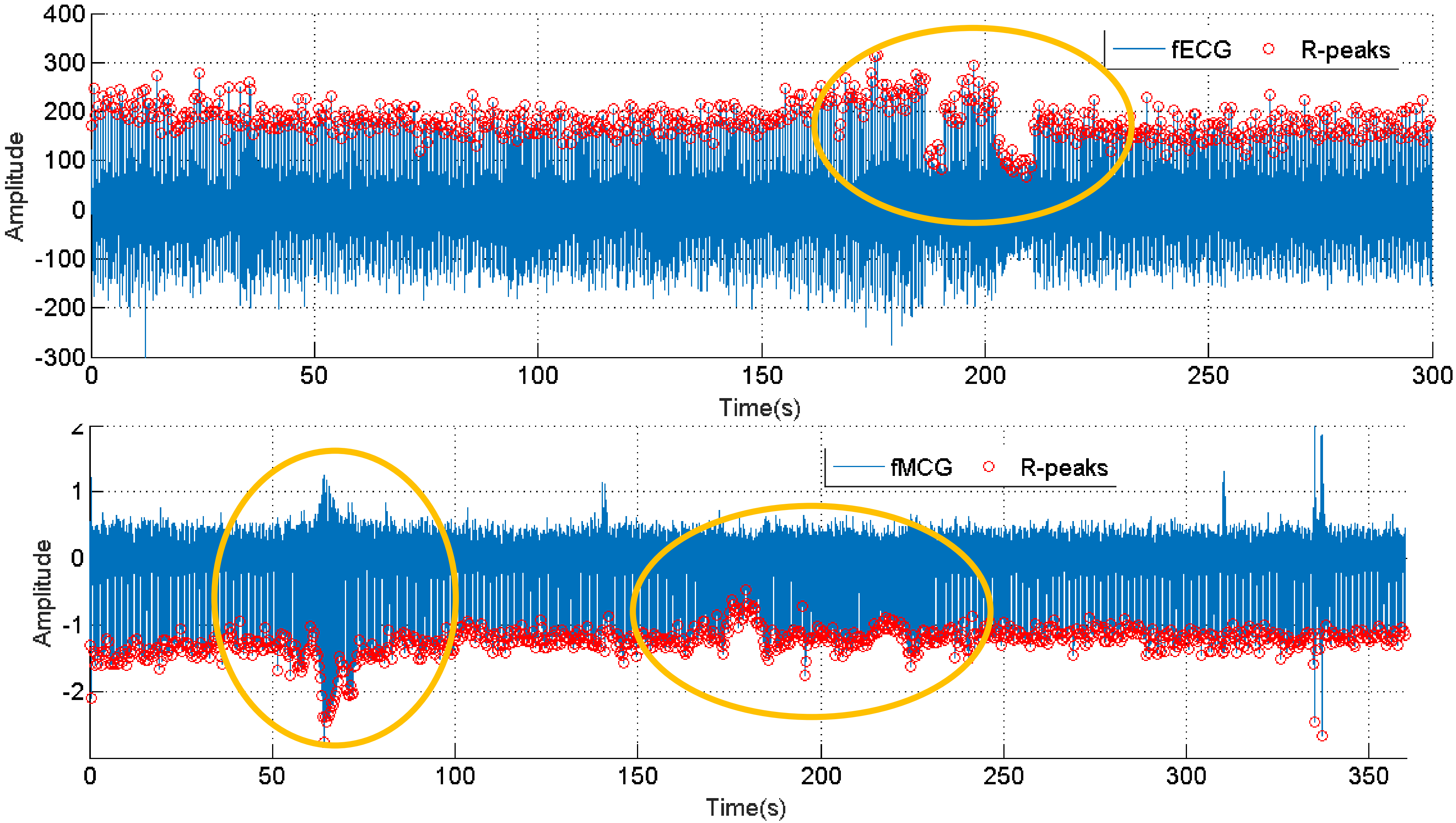
Time-Variant Scenarios

Example 2: Nonstationary case; minor fetal movement



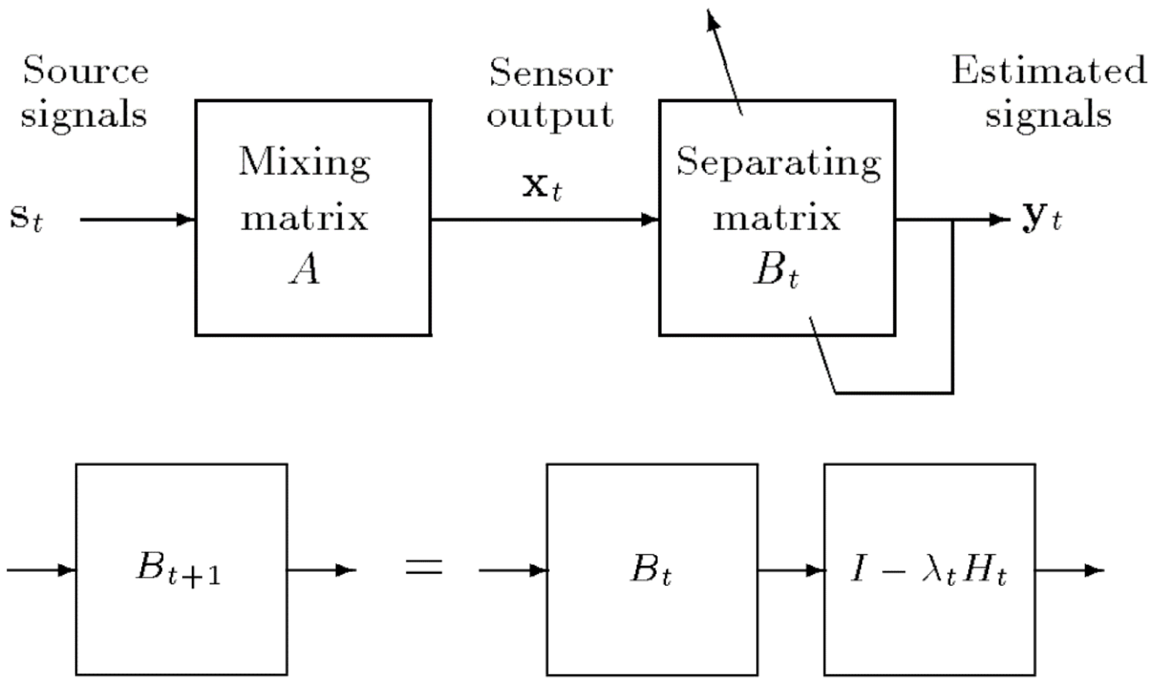
Time-Variant Scenarios

Example 3: Nonstationary case; significant fetal movement



Online Source Separation

- Solution: combining online tracking algorithms with blind source separation
- A well-known algorithm for online source separation is called equivariant adaptive separation via independence (EASI)
- This algorithm uses a serial (incremental) update of the demixing matrix as the new samples arrive

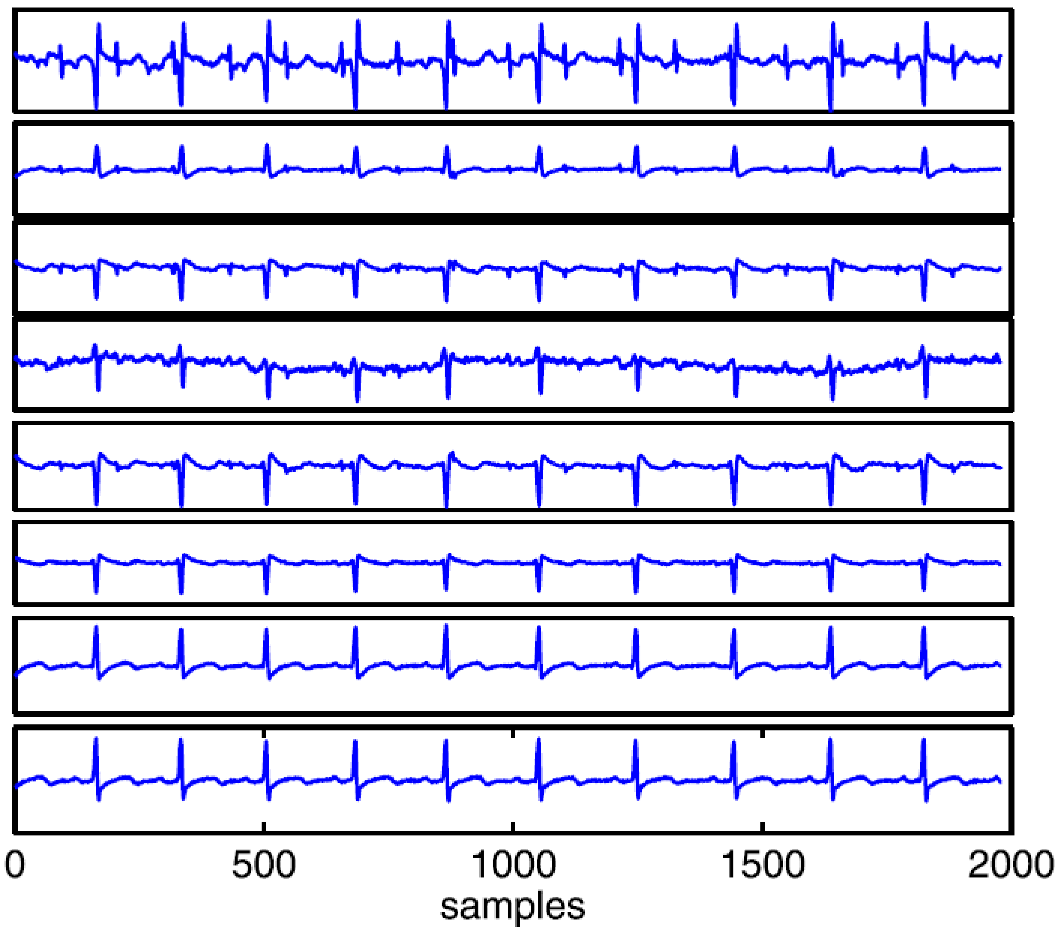


Ref: Cardoso, J. F., & Laheld, B. H. (1996). Equivariant adaptive source separation. *IEEE Transactions on signal processing*, *44*(12), 3017-3030.

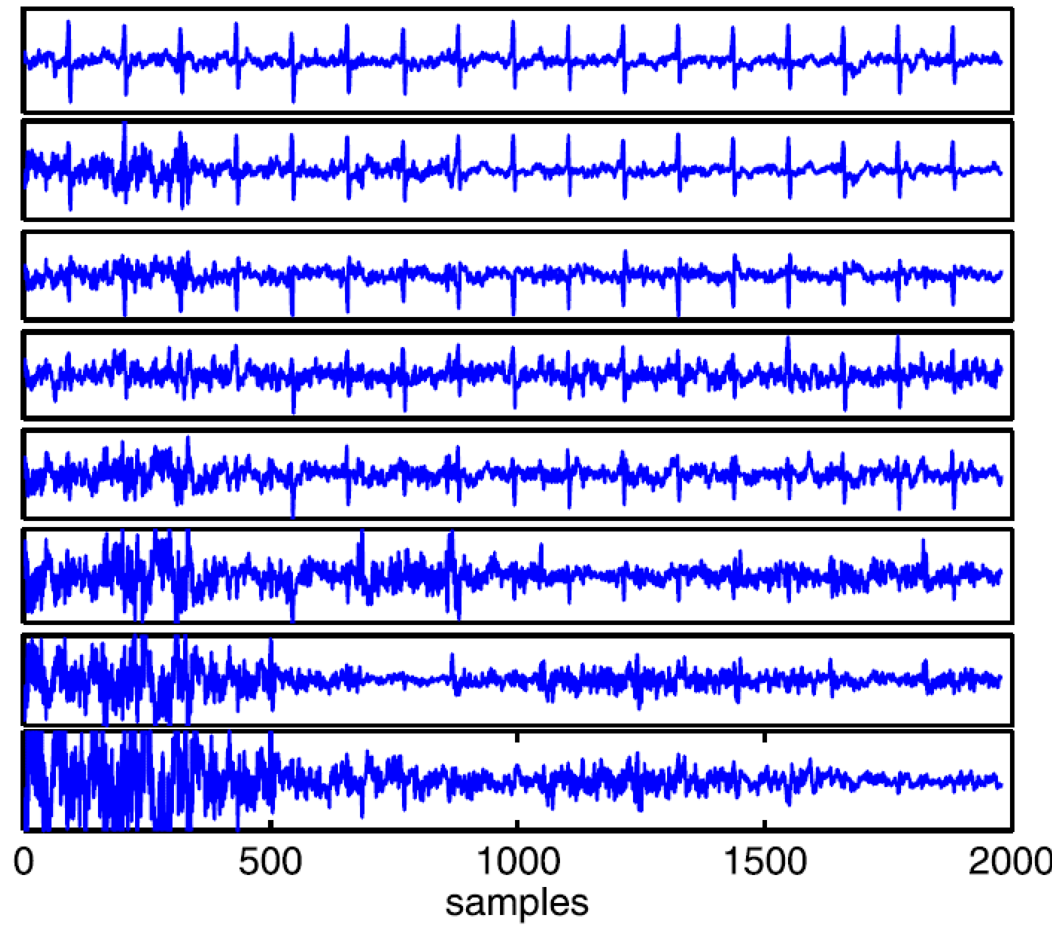
FECG Tracking using Online Deflation

Example:

Original data



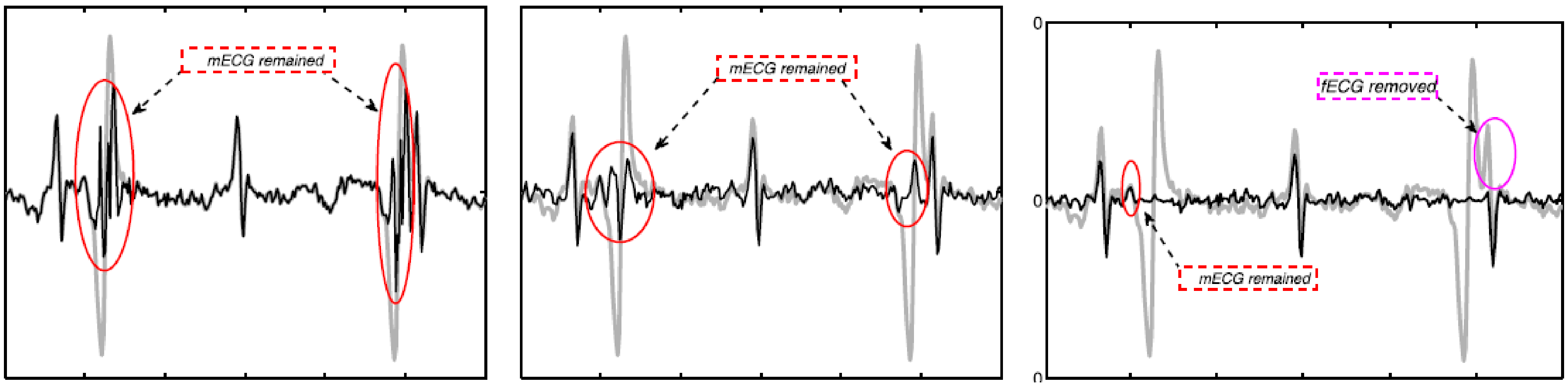
Online fECG extraction



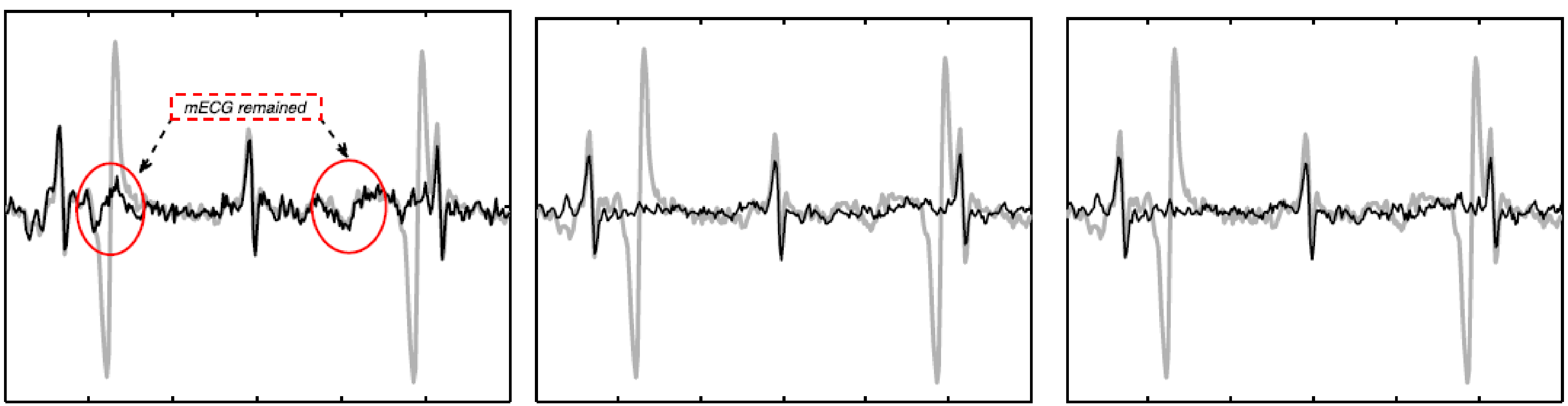
Ref: M. Fatemi and R. Sameni, “An Online Subspace Denoising Algorithm for Maternal ECG Removal from Fetal ECG Signals,” *Iranian Journal of Science and Technology, Transactions of Electrical Engineering*, vol. 2017, pp. 1-15, April 2017.

Comparison of Different Methods

Example:



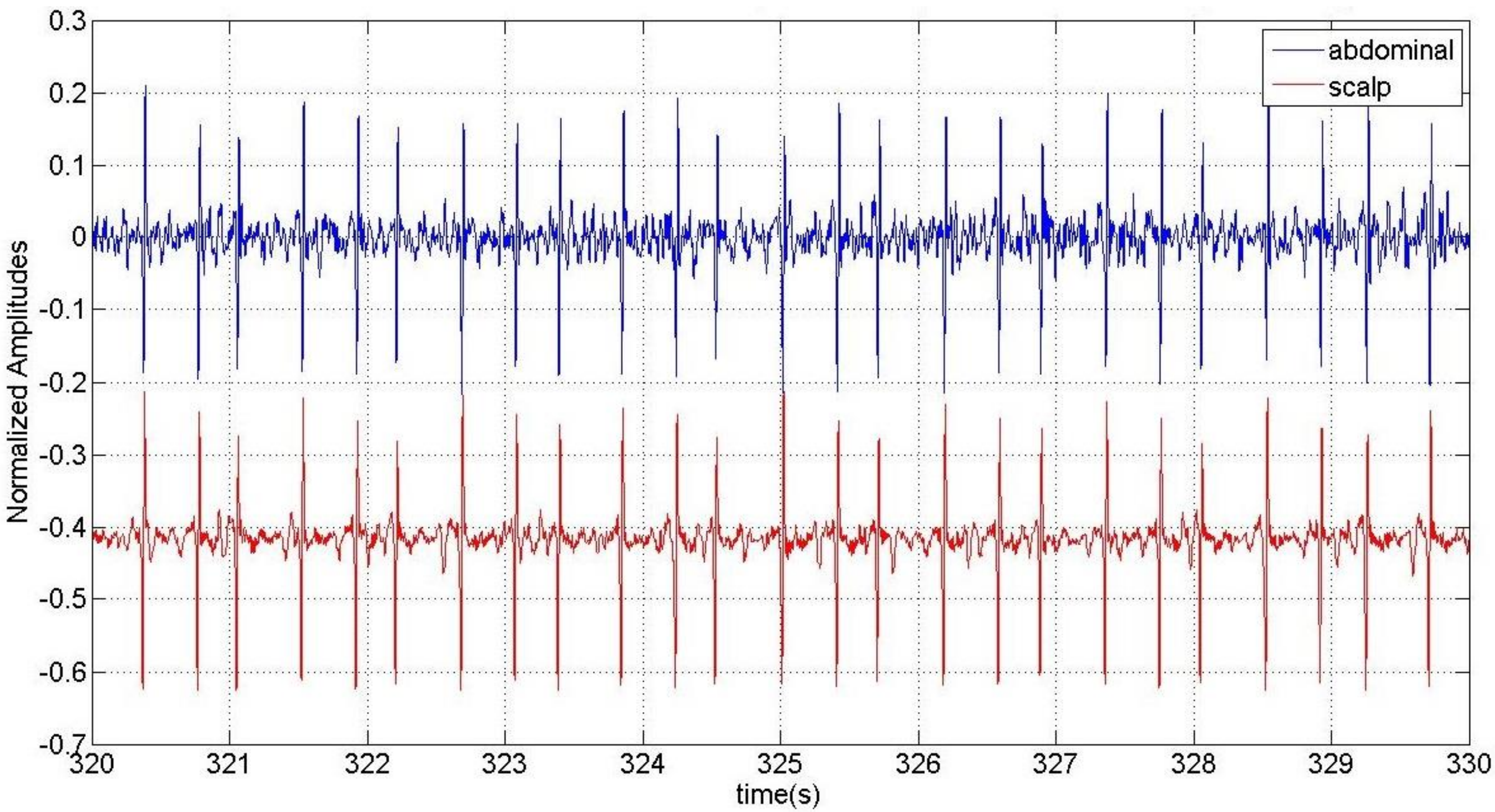
(a) ANC **(b)** Template subtraction **(c)** Kalman filter



(d) BSS **(e)** DEFL **(f)** ODEFL

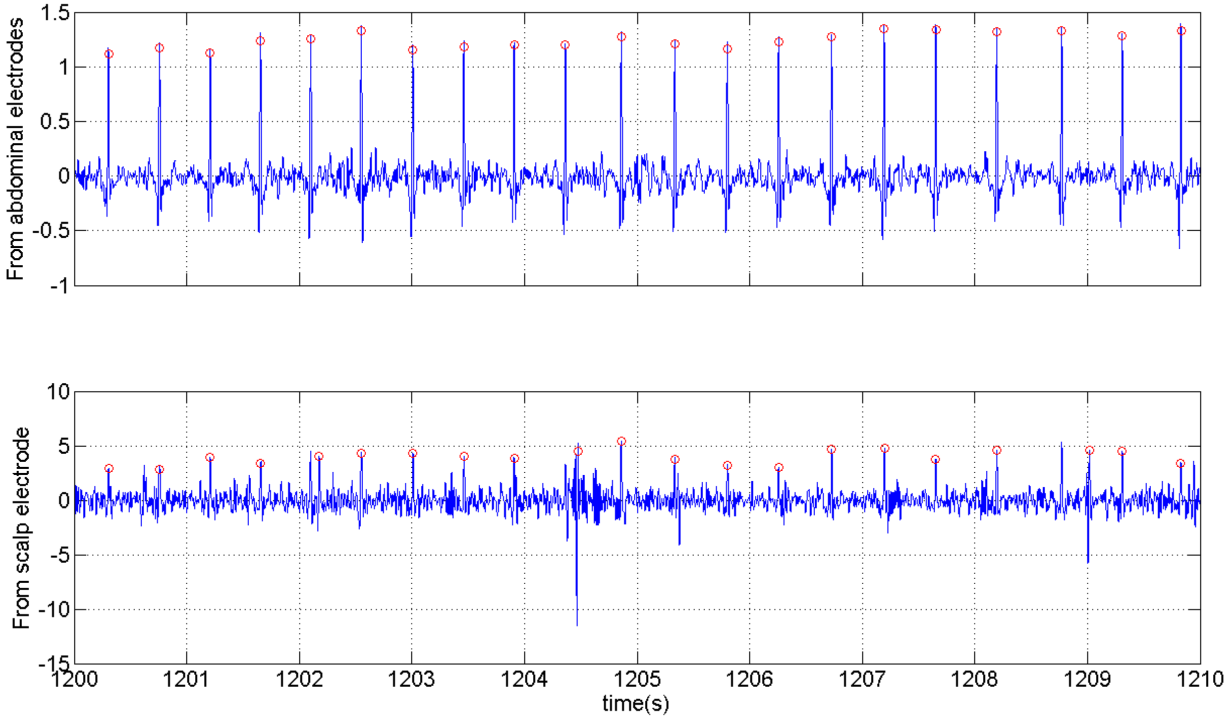
Maternal Abdominal vs. Fetal Scalp Lead FECG

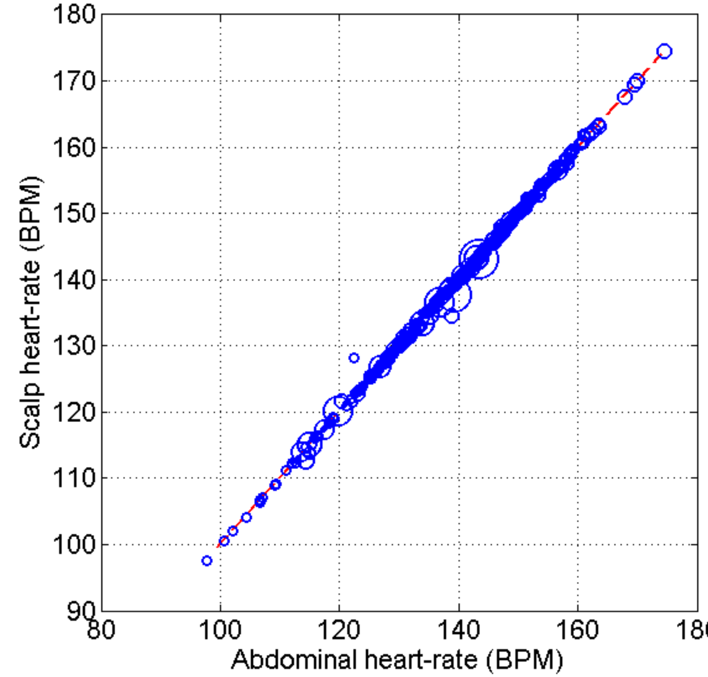
Example 1:



Maternal Abdominal vs. Fetal Scalp Lead Heart Rates

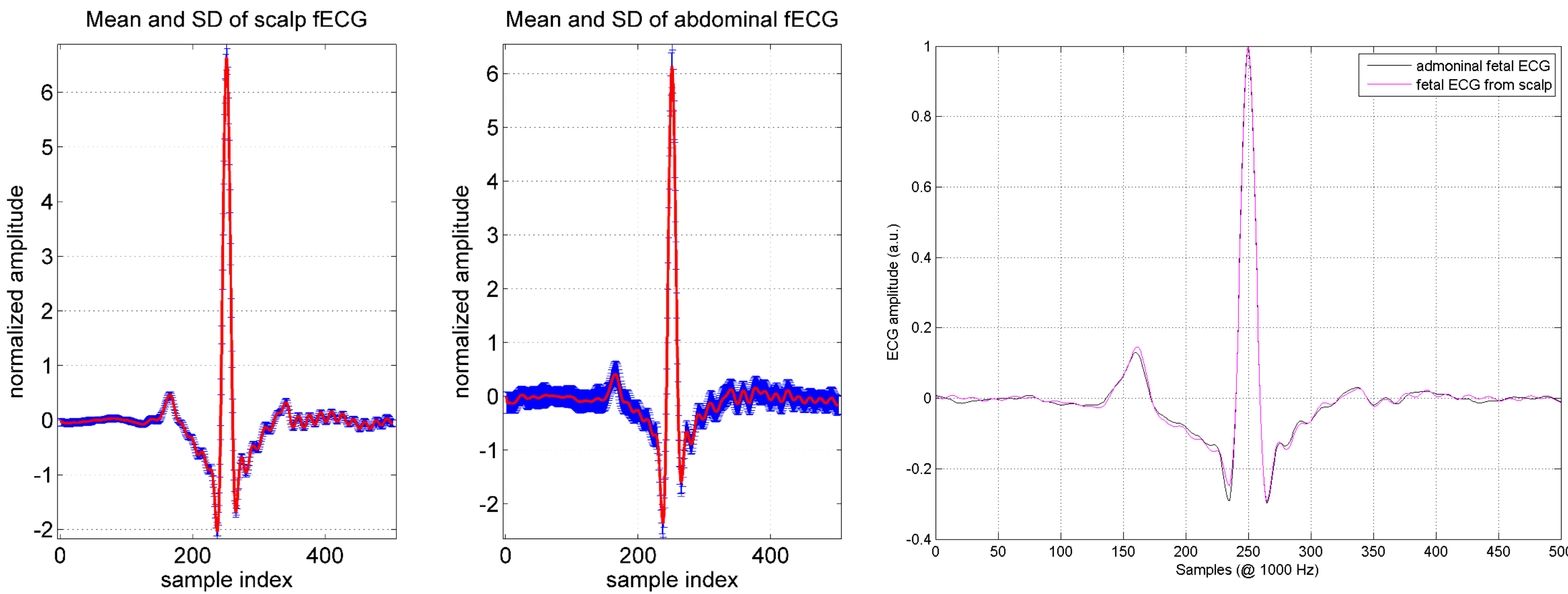
Example 2: The abdominal results may even be better than the scalp lead results in some cases





Maternal Abdominal vs. Fetal Scalp Lead Morphologies

Example 3:

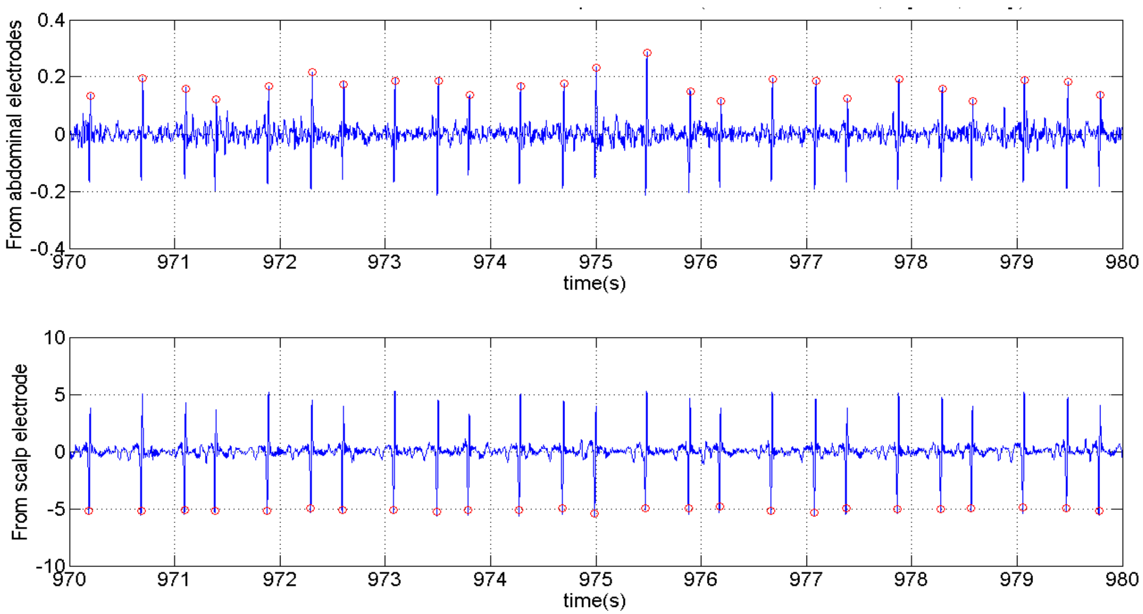


Question: Are the abdominal and scalp morphologies always identical?

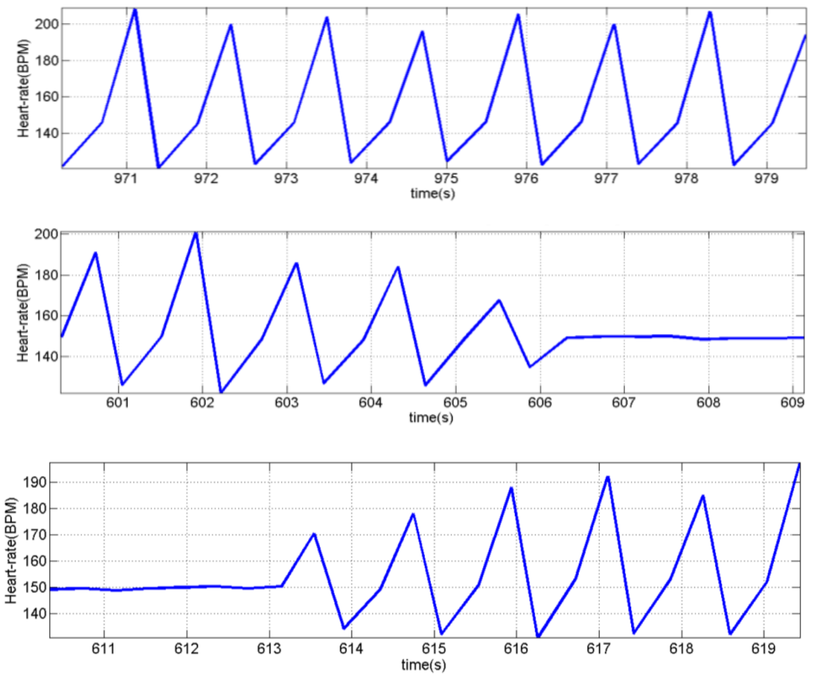
Ref: Clifford, G., Sameni, R., Ward, J., Robinson, J., & Wolfberg, A. J. (2011). Clinically accurate fetal ECG parameters acquired from maternal abdominal sensors. *American Journal of Obstetrics & Gynecology*, *205* (1), 47-e1.

Multiphasic Fetal Heart Rhythms

Example 4: Fetal heart rate time-series may demonstrate occasional multiphasic or chaotic behavior



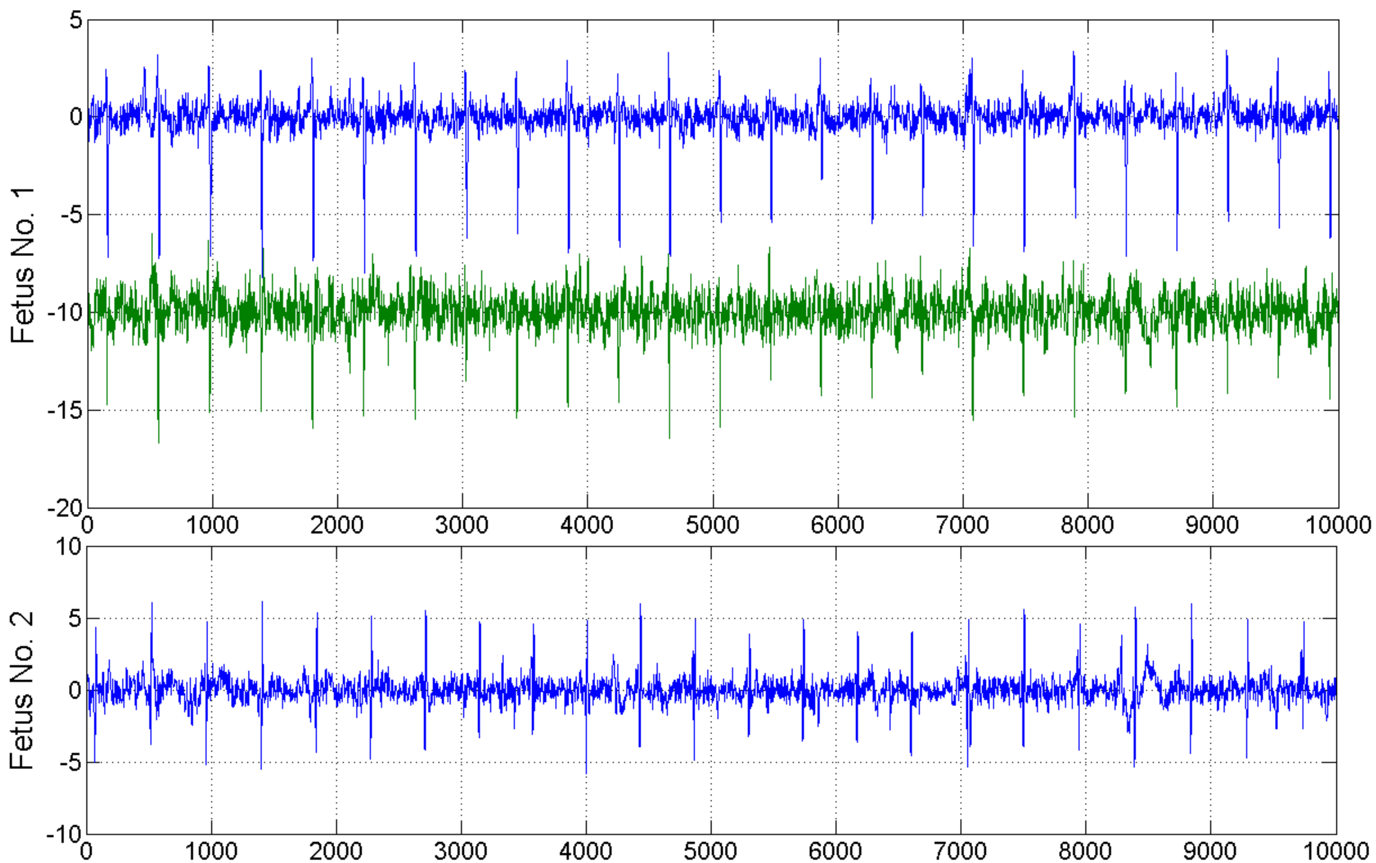
Extracted fECG



Heart-rate segments with multiphasic property

Multiple Pregnancies

Example 5: Twin fetuses MCG signals



Ref: Sameni, R. (2008). *Extraction of fetal cardiac signals from an array of maternal abdominal recordings* Doctoral dissertation, Institut National Polytechnique de Grenoble-INPG; Sharif University of Technology.

Advanced Blind Source Separation Methods

Current research and developments in our group for fetal cardiac signal extraction

Dynamic Source Separation

- Problem definition: We are focusing on a special class of semi-blind source separation problems, for which the sources are independent; but follow a presumed dynamics:

$$\boldsymbol{s}_{t+1} = \boldsymbol{f}(\boldsymbol{s}_t, \boldsymbol{w}_t)$$
$$\boldsymbol{x}_t = \boldsymbol{h}(\boldsymbol{s}_t) + \boldsymbol{n}_t$$

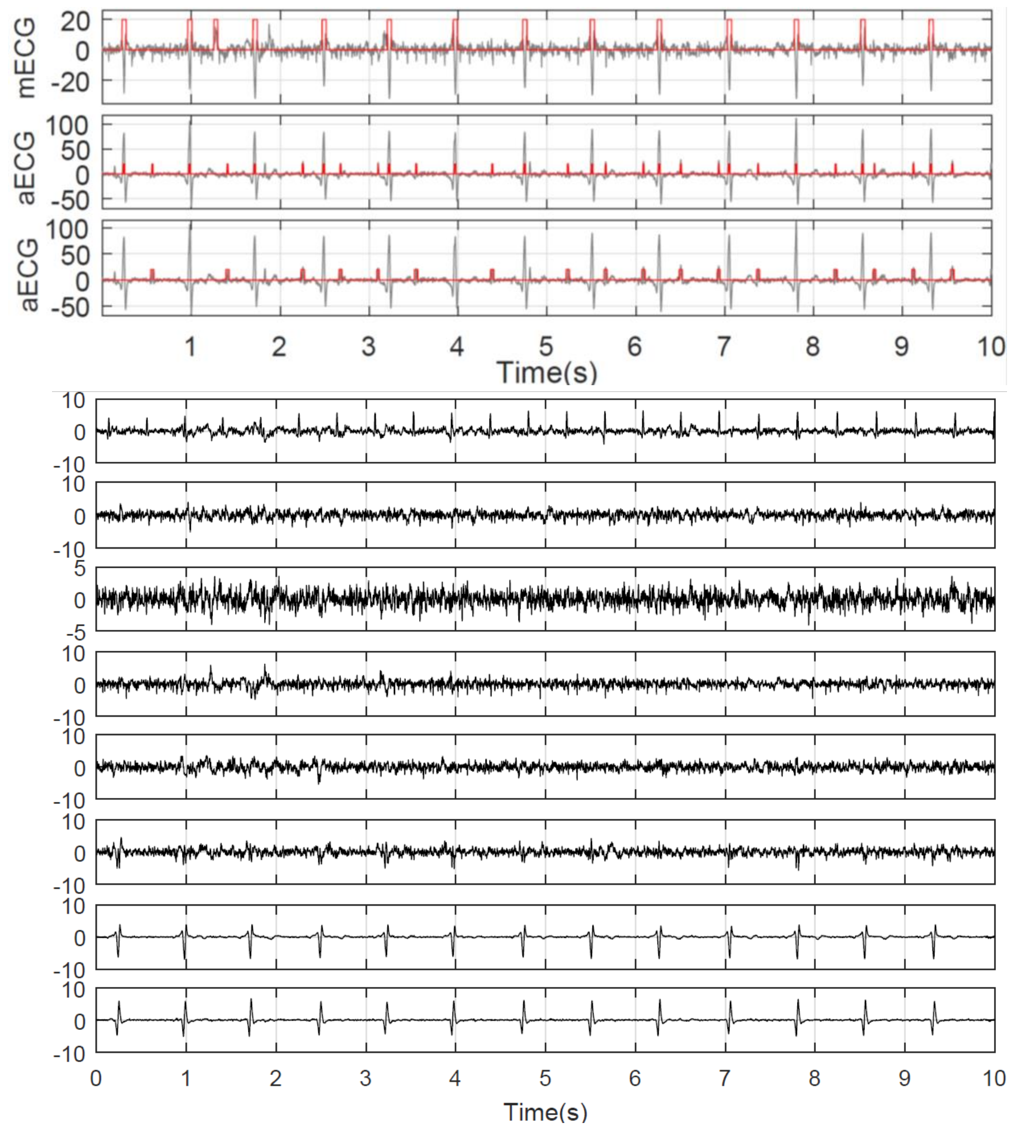
- Assumptions:
- $\boldsymbol{w}_t \in \mathbb{R}^{\boldsymbol{M}}$ is a vector of M white independent sources of model noise
- $\boldsymbol{n}_t \in \mathbb{R}^{\boldsymbol{N}}$ is the observation noise, independent from $\boldsymbol{w}_t$
- $\boldsymbol{f}(\cdot)$ is known (or presumed)
- $\boldsymbol{h}(\cdot)$ is unknown
- $\boldsymbol{s}_t \in \mathbb{R}^{\boldsymbol{P}}$ is the state vector of interest
- $\boldsymbol{x}_t \in \mathbb{R}^{\boldsymbol{N}}$ is the observation vector

- Objective: Retrieve the sources $\boldsymbol{s}_t$ by implicit or explicit estimation and inversion of $\boldsymbol{h}(\cdot)$
- Methodology: We are focusing on the properties of the innovation process to design source separation algorithms for random processes

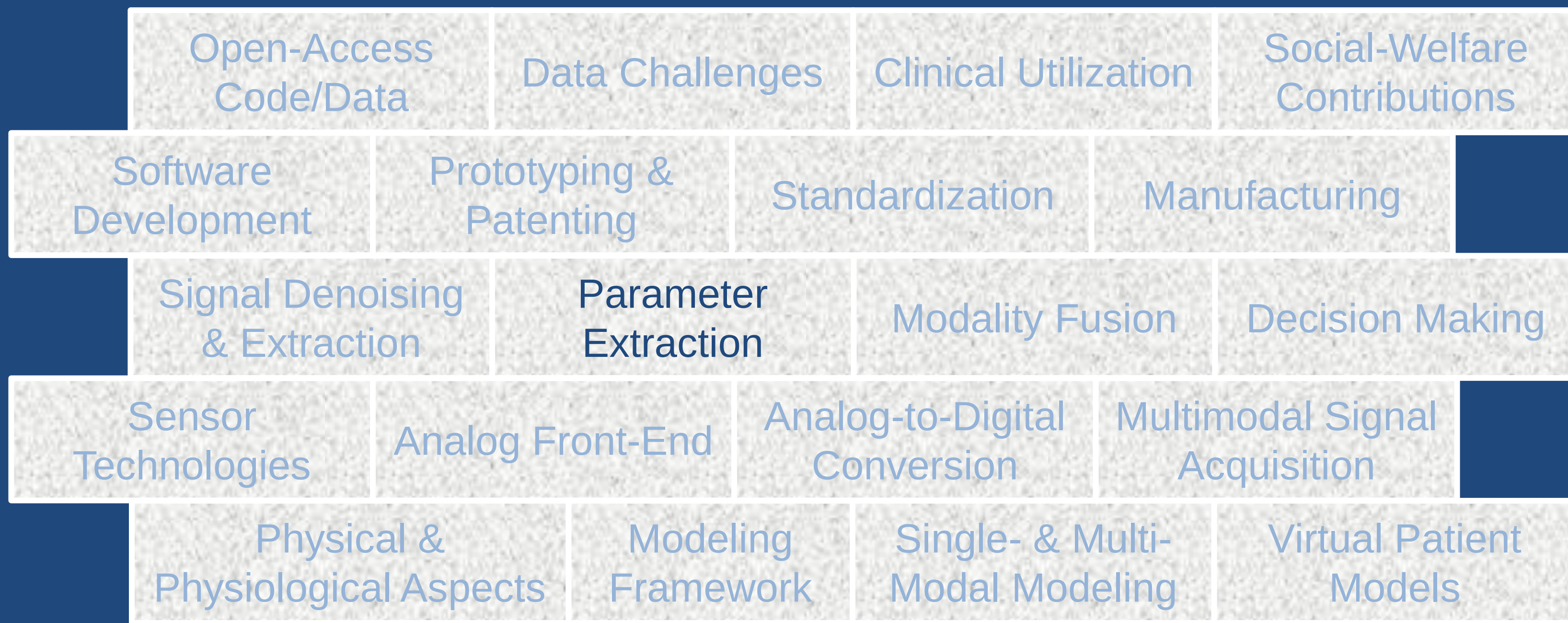
Nonstationary Component Analysis

- Idea: detecting segments of nonstationary using a hypothesis test over the signal or its innovations (unpredictable parts):

$$\mathcal{H}_0: \quad \tilde{\boldsymbol{v}}(t) = \hat{\boldsymbol{\eta}}(t)$$
$$\mathcal{H}_1: \quad \tilde{\boldsymbol{v}}(t) = \hat{\boldsymbol{\eta}}(t) + \mathbf{n}(t)$$



Ref: Fahimeh Jamshidian-Tehrani, Reza Sameni, and Christian Jutten, "Temporally Nonstationary Component Analysis; Application to Noninvasive Fetal Electrocardiogram Extraction", Submitted to *IEEE Transactions on Biomedical Engineering*, 2019



Post-fetal ECG extraction clinical parameter calculation

Fetal ECG Parameters

As with adult ECG, clinical information regarding the fetal heart is embedded in the heart rate and morphology of the fetal ECG:

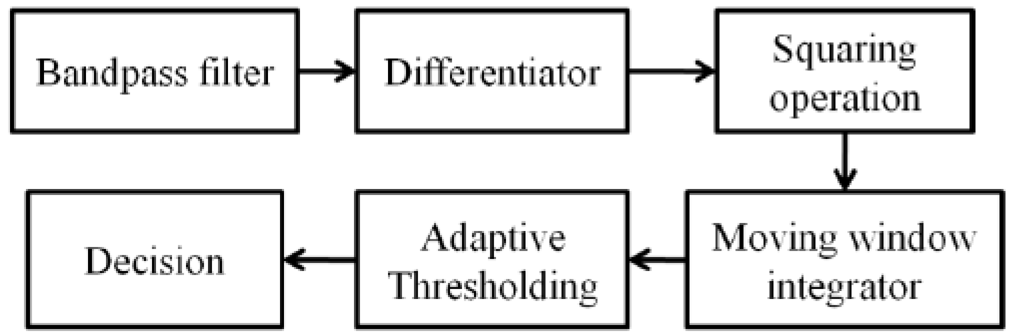
1. Heart-rate: Obtained by robust R-peak detection, requires rule-based refinements (correcting excess/missing beats)
2. Morphology: Fetal ECG morphologic parameters are commonly extracted by robust synchronous averaging to improve the SNR

Refer to: The Noninvasive Fetal ECG: the PhysioNet/Computing in Cardiology Challenge 2013: Silva, I., Behar, J., Sameni, R., Zhu, T., Oster, J., Clifford, G. D., & Moody, G. B. (2013, September). Noninvasive fetal ECG: the PhysioNet/computing in cardiology challenge 2013. In *Computing in Cardiology Conference (CinC), 2013* (pp. 149-152). IEEE.

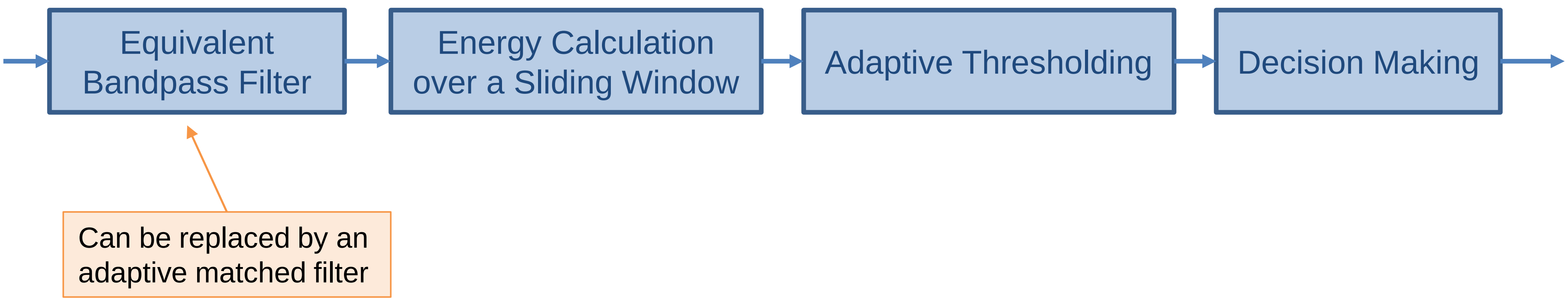
Robust R-Peak Detector

- The Pan & Tompkins R-peak detector (1985)

Basic block diagram:



Simplified diagram:



The Pan-Tompkins method: Pan, Jiapu, and Willis J. Tompkins. "A real-time QRS detection algorithm." *IEEE Trans. Biomed. Eng* 32.3 (1985): 230-236.
Robust matched filter: Jamshidian-Tehrani, Fahimeh, and Reza Sameni. "Fetal ECG extraction from time-varying and low-rank noninvasive maternal abdominal recordings." *Physiological measurement* 39.12 (2018): 125008.

Fetal Heart Rate Correction

Example: Conditional median filtering for refining the heart-rate sequence

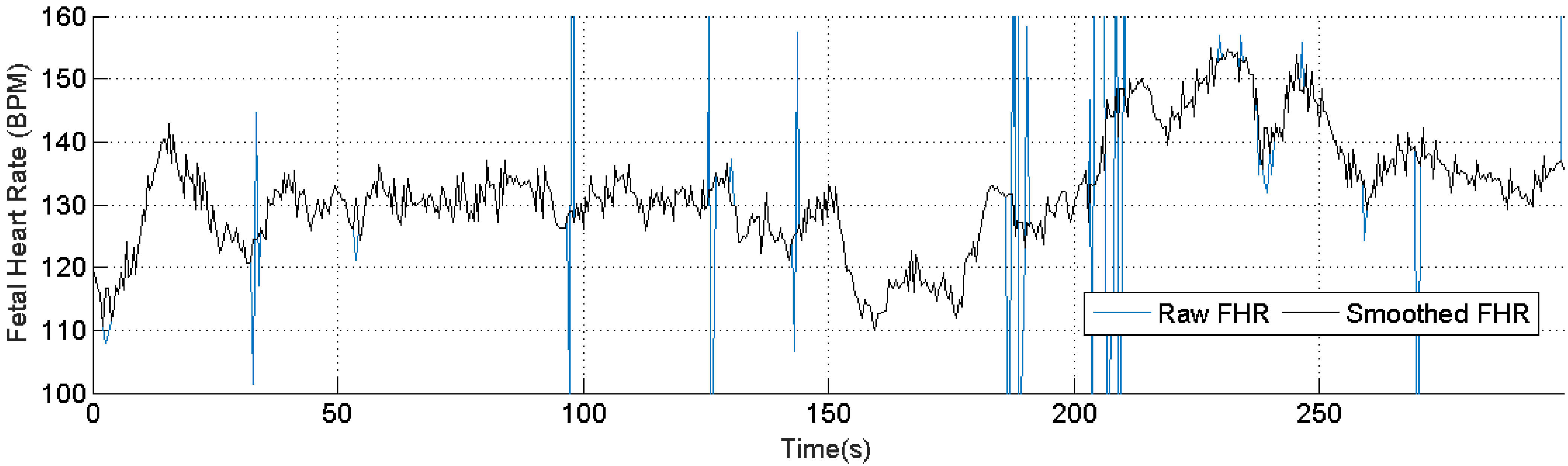
```
for n = 1,2,…,N
   med[n] = MEDIAN(HR[n-w], HR[n-w+1], …, HR[n+w])
   if(|HR[n] - med[n]| > Threshold)
       HRc[n] = med[n];
   else
       HRc[n] = HR[n];
 end
```

- This filter is nonlinear; it retains the HR sequence unchanged during normal segments and only smoothens the outliers.

Ref: Jamshidian-Tehrani, Fahimeh, and Reza Sameni. "Fetal ECG extraction from time-varying and low-rank noninvasive maternal abdominal recordings." *Physiological measurement* 39.12 (2018): 125008.
Further reading on nonlinear filters: Arce, G. R. (2005). *Nonlinear signal processing: a statistical approach*. John Wiley & Sons.

Fetal Heart Rate Correction (continued)

Example 1: Fetal ECG refining



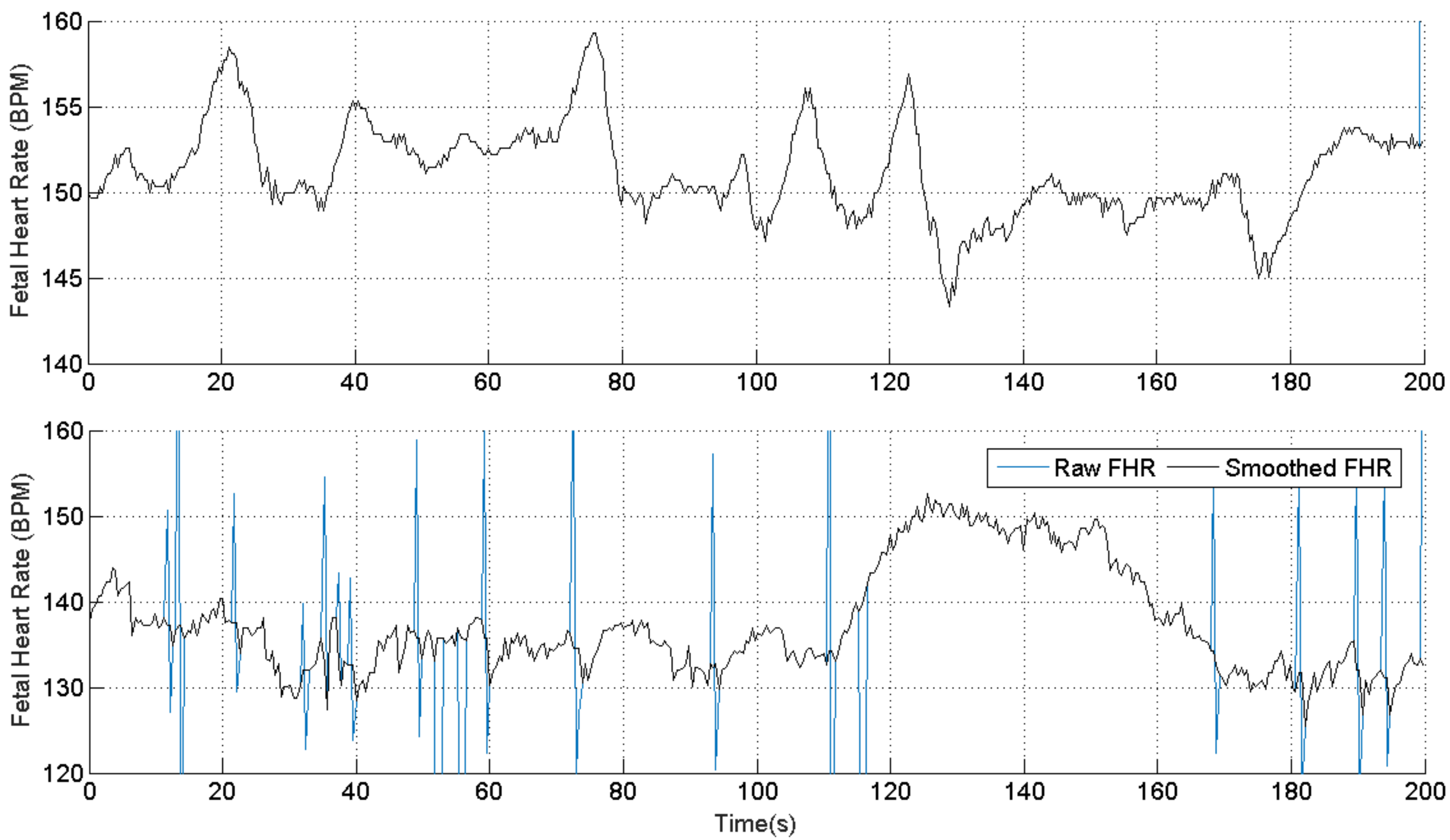
Ref: H. Biglari and R. Sameni, “Fetal motion estimation from noninvasive cardiac signal recordings,” *Physiological Measurement*, vol. 37, no. 11, pp. 2003-2023, November 2016.

Fetal Heart Rate Correction (continued)

Example 2: Twin fetuses (MCG data)

Fetus 1

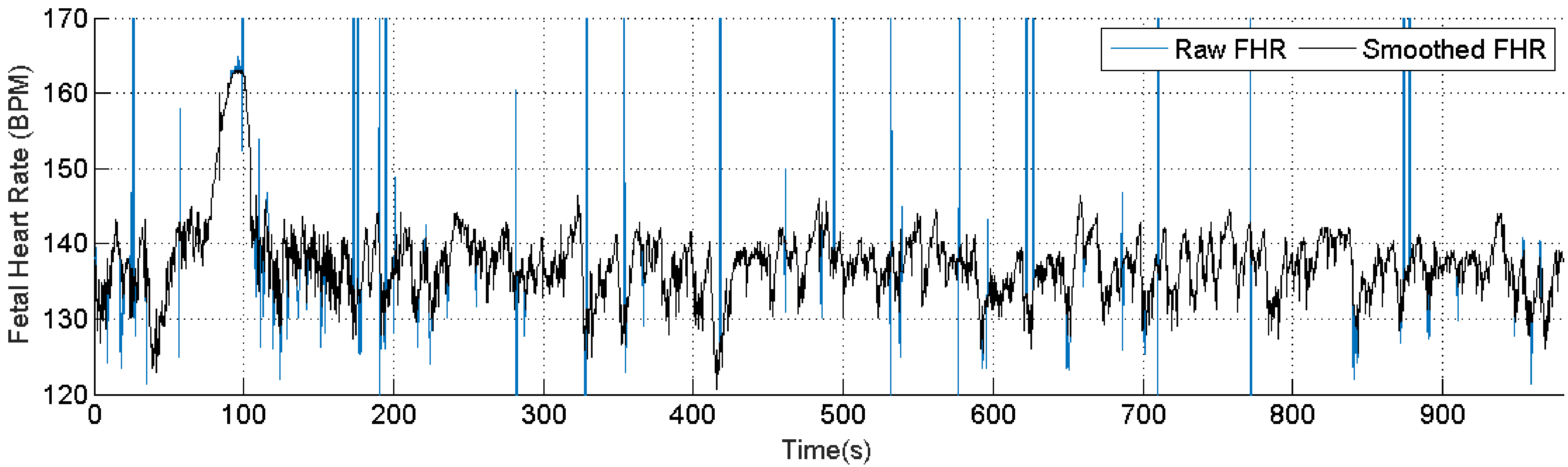
Fetus 2



Ref: H. Biglari and R. Sameni, "Fetal motion estimation from noninvasive cardiac signal recordings," *Physiological Measurement*, vol. 37, no. 11, pp. 2003-2023, November 2016.

Fetal Heart Rate Correction (continued)

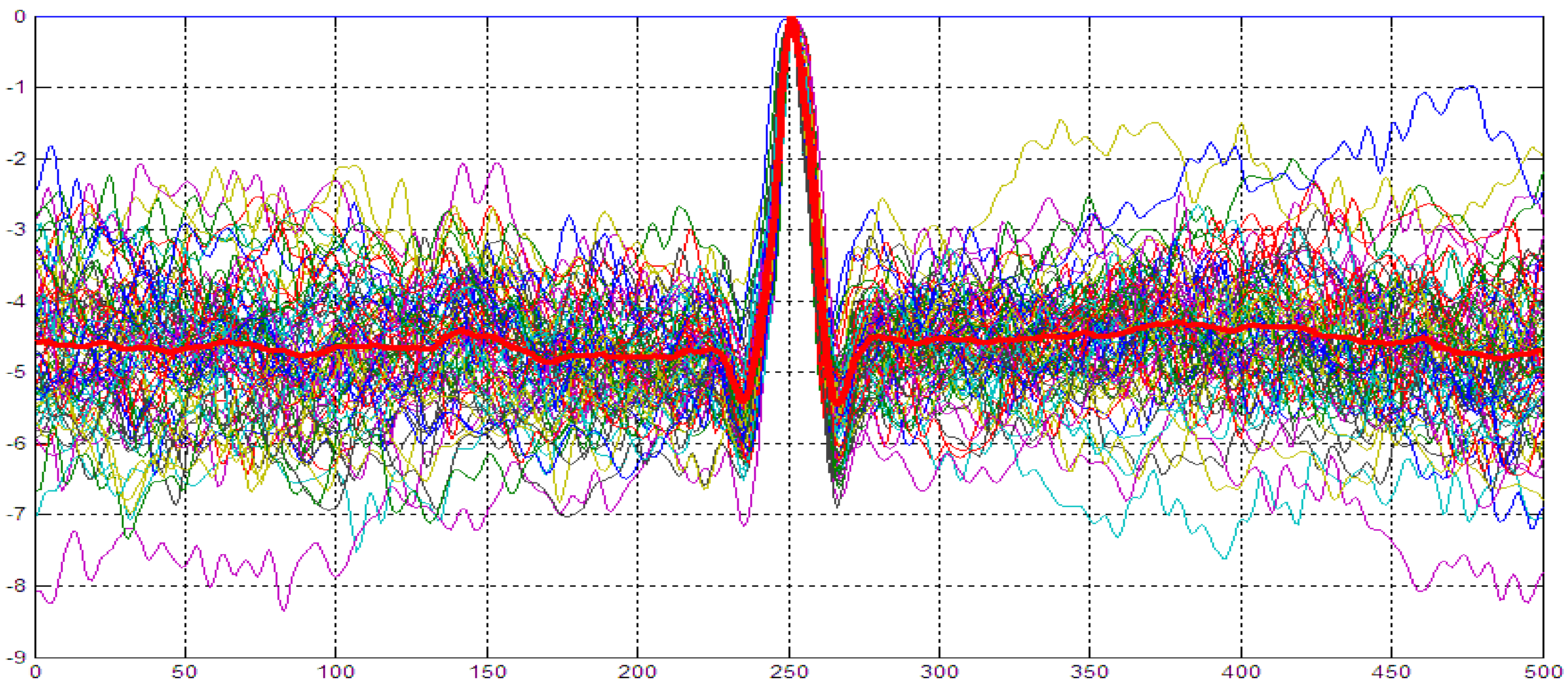
Example 3: Fetal ECG refining



Ref: H. Biglari and R. Sameni, “Fetal motion estimation from noninvasive cardiac signal recordings,” *Physiological Measurement*, vol. 37, no. 11, pp. 2003-2023, November 2016.

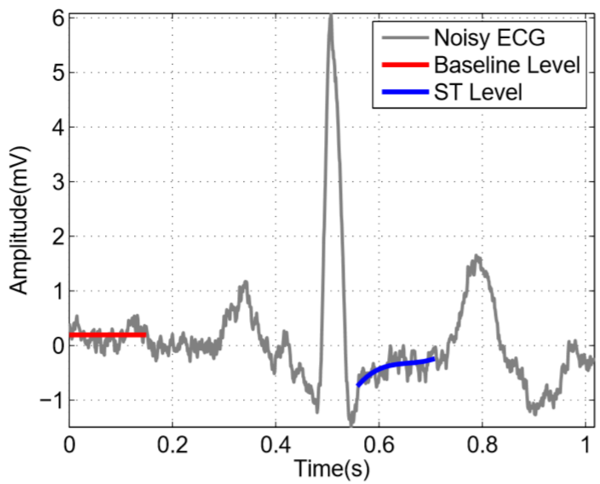
Fetal Morphologic Parameters

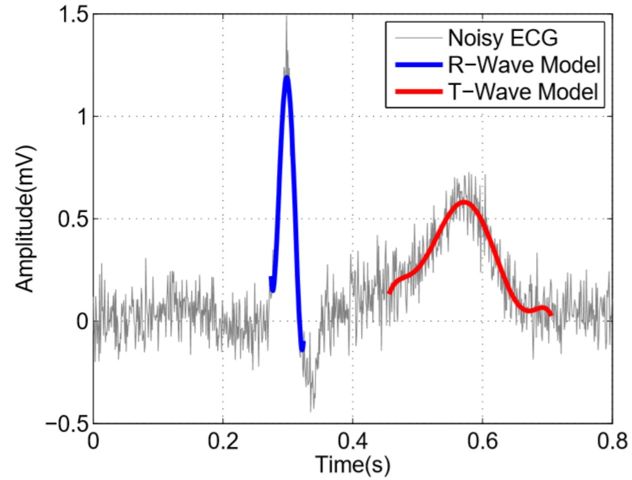
- Average beat morphologies are obtained by beat alignment and (weighted) averaging.
- The beat averaging can either be simple or normalized by the RR-intervals

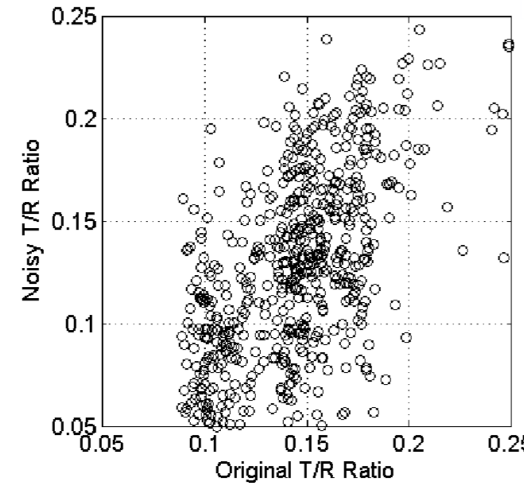


Model-Based ECG Parameter Extraction

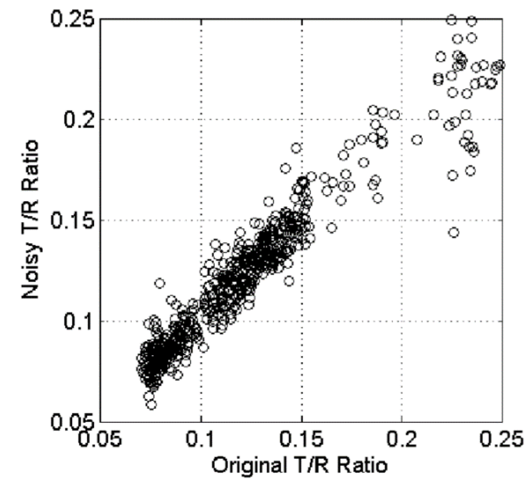
- By model fitting over adult/fetal ECG segments, more accurate and robust parameters are obtained







without model fitting

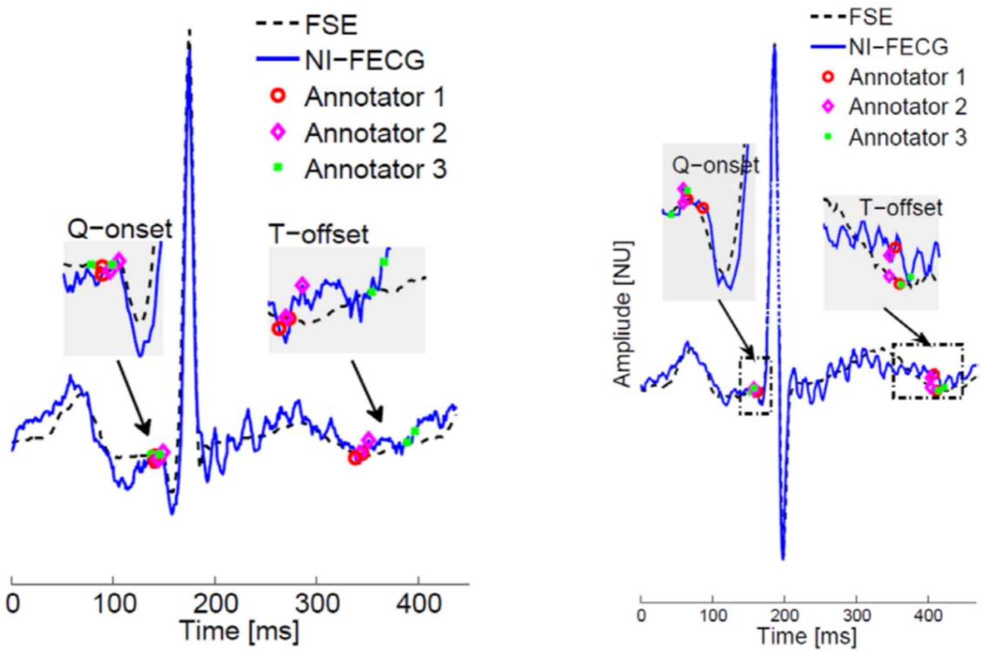


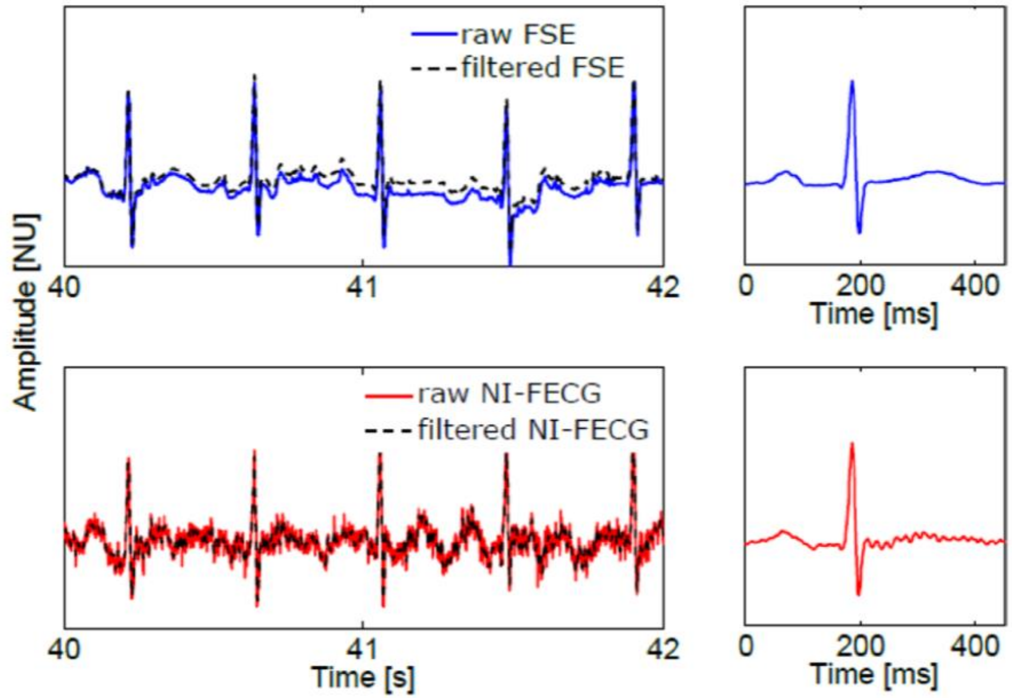
with model fitting

Currently ongoing research; images subject to copyright

Fetal QT Interval

Example:

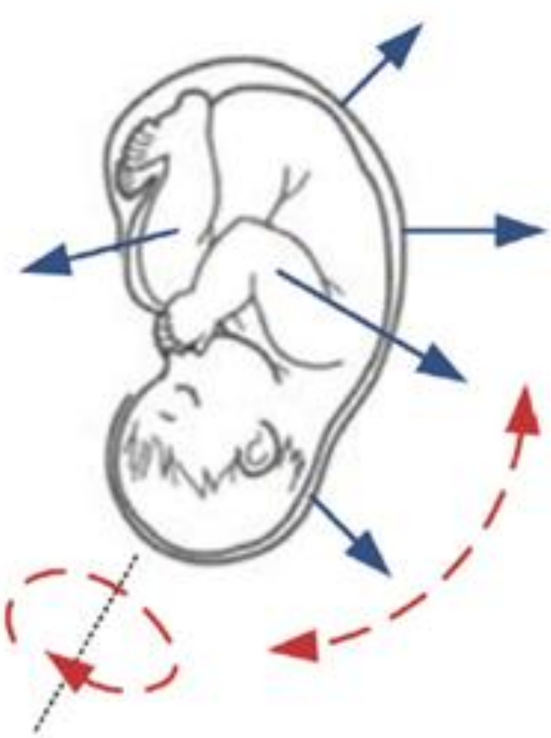




Ref: J. Behar, T. Zhu, J. Oster, A. Niksch, D. Y. Mah, T. Chun, J. Greenberg, C. Tanner, J. Harrop, R. Sameni, J. Ward, A. J. Wolfberg, and G. D. Clifford, “Evaluation of the fetal QT interval using non-invasive fetal ECG technology,” *Physiological Measurement*, vol. 37, no. 9, pp. 1392-1403, September 2016.

Complementary FECG-Inferred Information

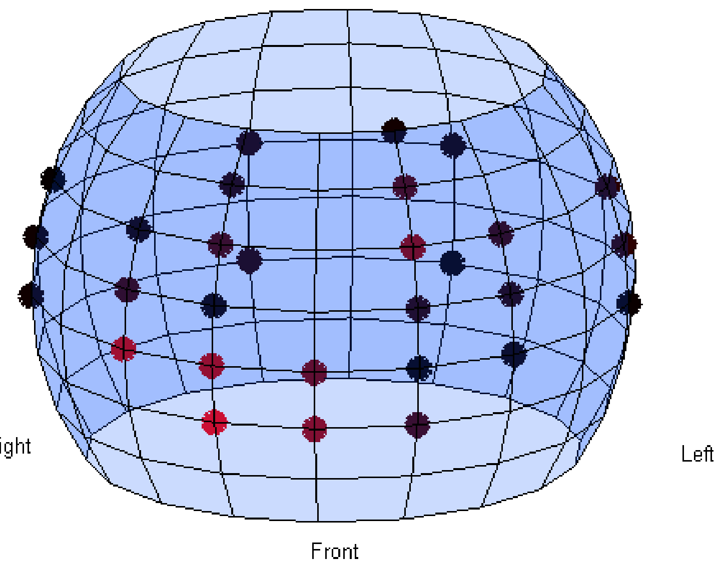
- The extracted fetal ECG can be used to extract complementary information regarding the fetal well-being (beyond the fetal heart)
- Examples:
  - Fetal motion tracking
  - Fetal position with respect to the maternal body coordinates



Ref: Vullings, R., Peters, C. H. L., Mischi, M., Oei, S. G., & Bergmans, J. W. M. (2008, August). Fetal movement quantification by fetal vectorcardiography: a preliminary study. In *Engineering in Medicine and Biology Society, 2008. EMBS 2008. 30th Annual International Conference of the IEEE* (pp. 1056-1059). IEEE.

Fetal Position Extraction

- By mapping the fECG back to the abdominal lead space and calculating the energy distribution of the fECG across the abdominal leads an estimate of the fetal position is obtained
- By mapping the beats onto a "canonical representation" the fetal orientation with respect to the maternal body is obtained ► *standard fetal ECG*



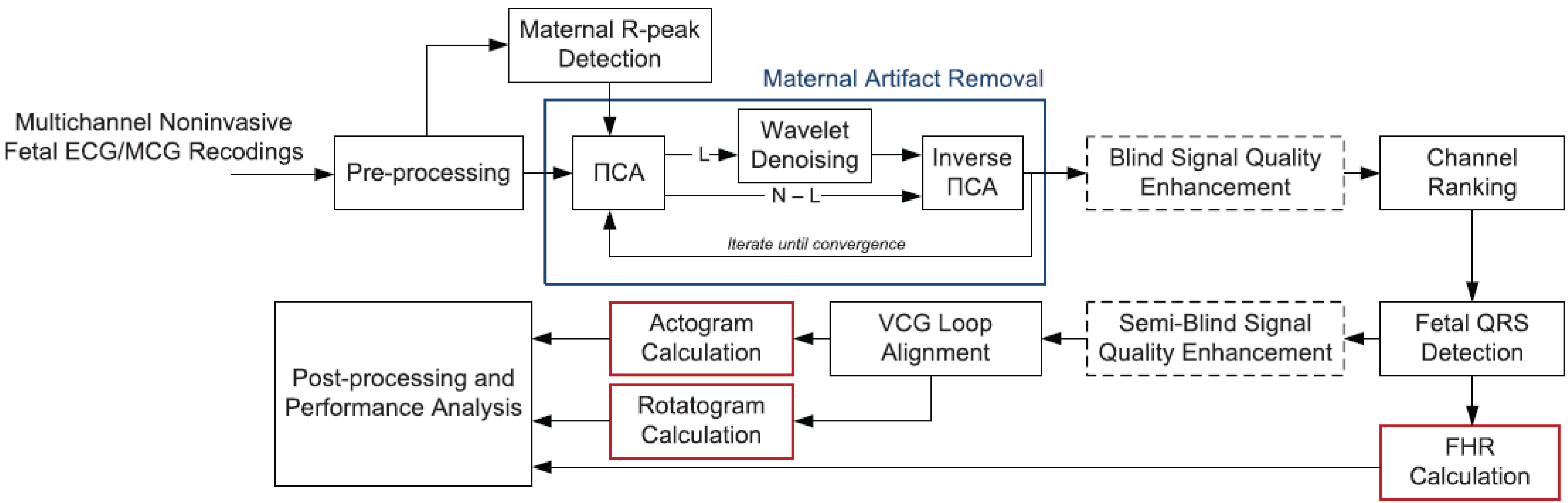
This method has also been evaluated over noninvasive fetal Magnetoencephalogram!

Refs:

- Clifford, G., Sameni, R., Ward, J., Robinson, J., & Wolfberg, A. J. (2011). Clinically accurate fetal ECG parameters acquired from maternal abdominal sensors. *American Journal of Obstetrics & Gynecology*, *205*(1), 47-e1.
- Razavipour, Fatemeh, and Reza Sameni. "A general framework for extracting fetal magnetoencephalogram and audio-evoked responses." *Journal of neuroscience methods* 212.2 (2013): 283-296.

Fetal Motion Tracking from fECG

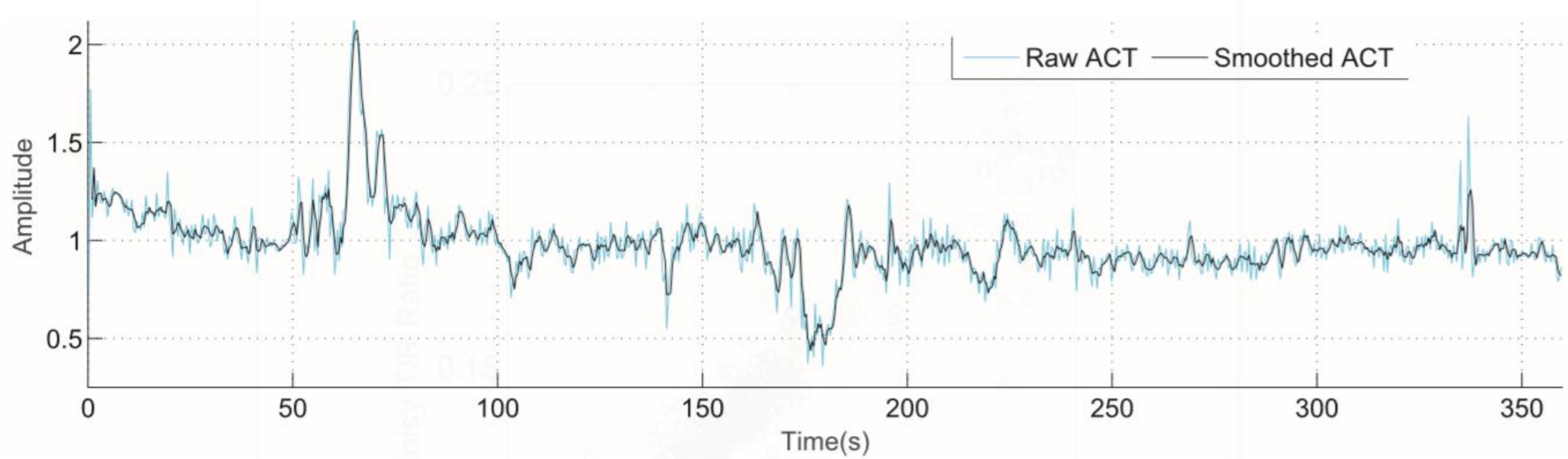
The notion of fetal actogram and rotatogram using fECG beat alignment:

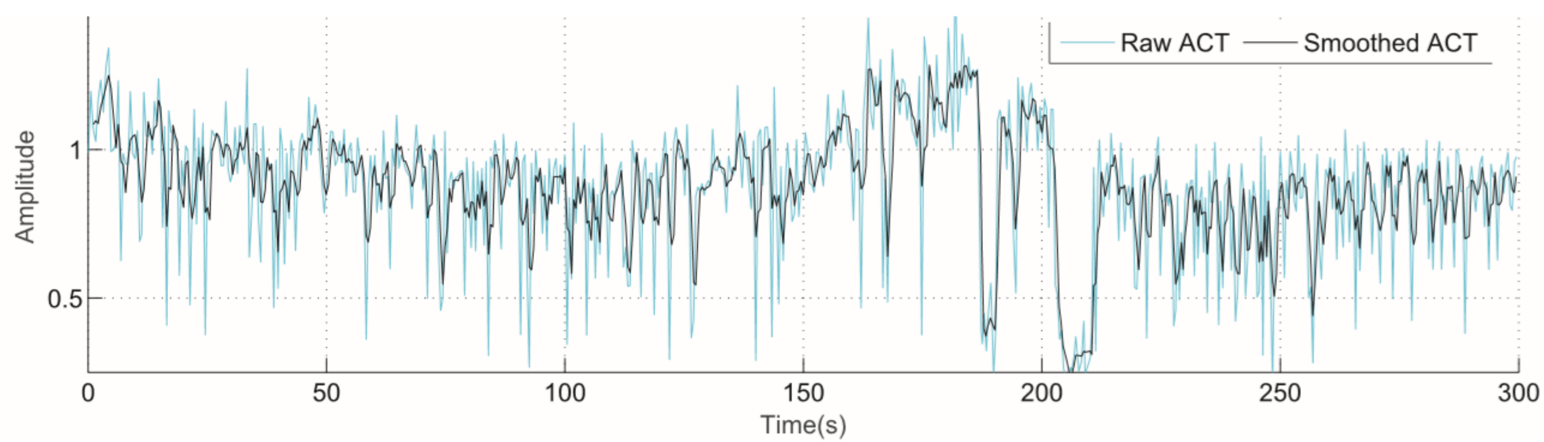


Ref: H. Biglari and R. Sameni, "Fetal motion estimation from noninvasive cardiac signal recordings," *Physiological Measurement*, vol. 37, no. 11, pp. 2003-2023, November 2016.

Fetal Motion Tracking from fECG (continued)

Example:





Ref: H. Biglari and R. Sameni, “Fetal motion estimation from noninvasive cardiac signal recordings,” *Physiological Measurement*, vol. 37, no. 11, pp. 2003-2023, November 2016.

Open-Access Code/Data | Data Challenges | Clinical Utilization | Social-Welfare Contributions

Software Development | Prototyping & Patenting | Standardization | Manufacturing

Signal Denoising & Extraction | Parameter Extraction | **Modality Fusion** | Decision Making

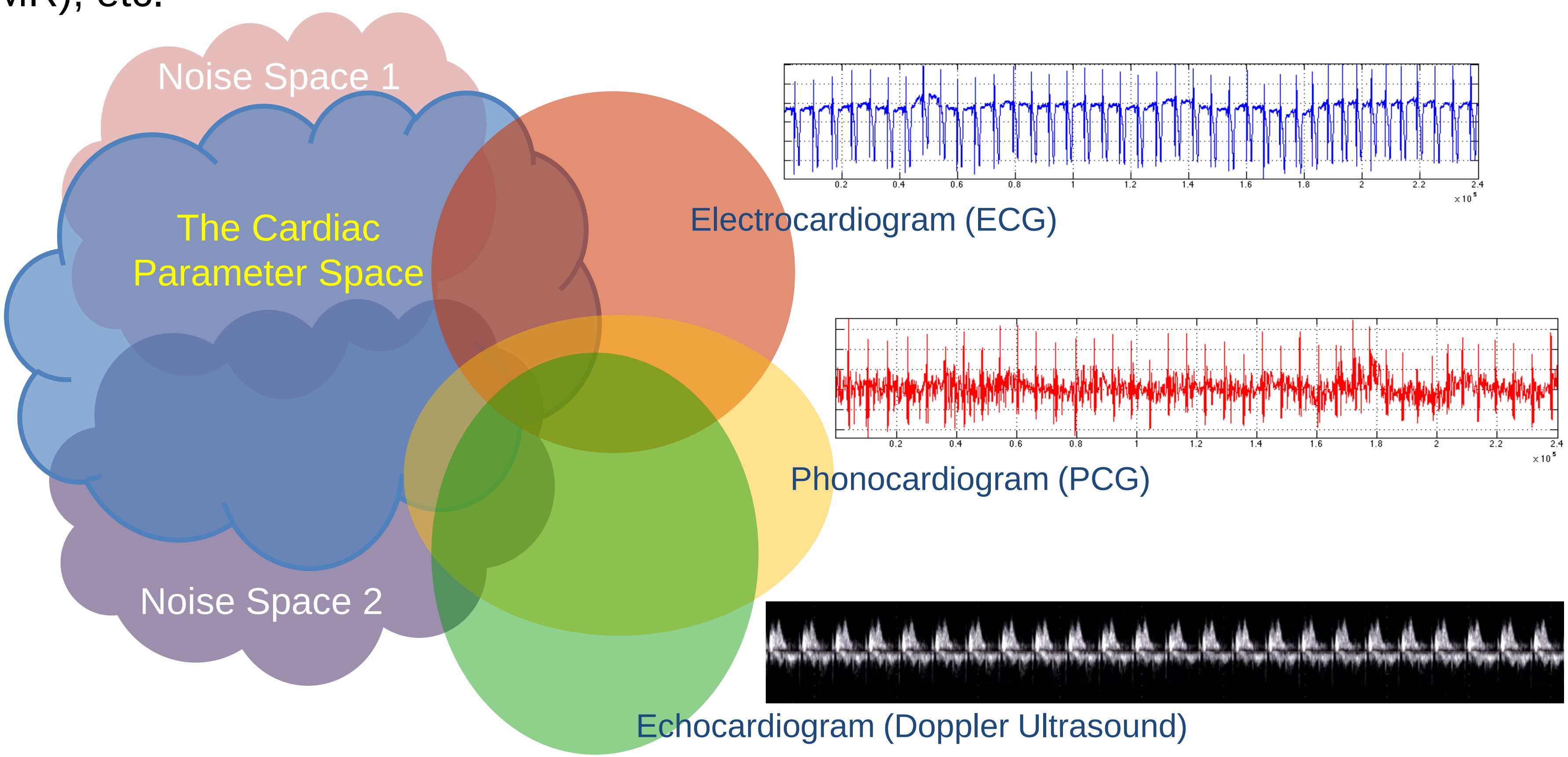
Sensor Technologies | Analog Front-End | Analog-to-Digital Conversion | Multimodal Signal Acquisition

Physical & Physiological Aspects | Modeling Framework | Single- & Multi-Modal Modeling | Virtual Patient Models

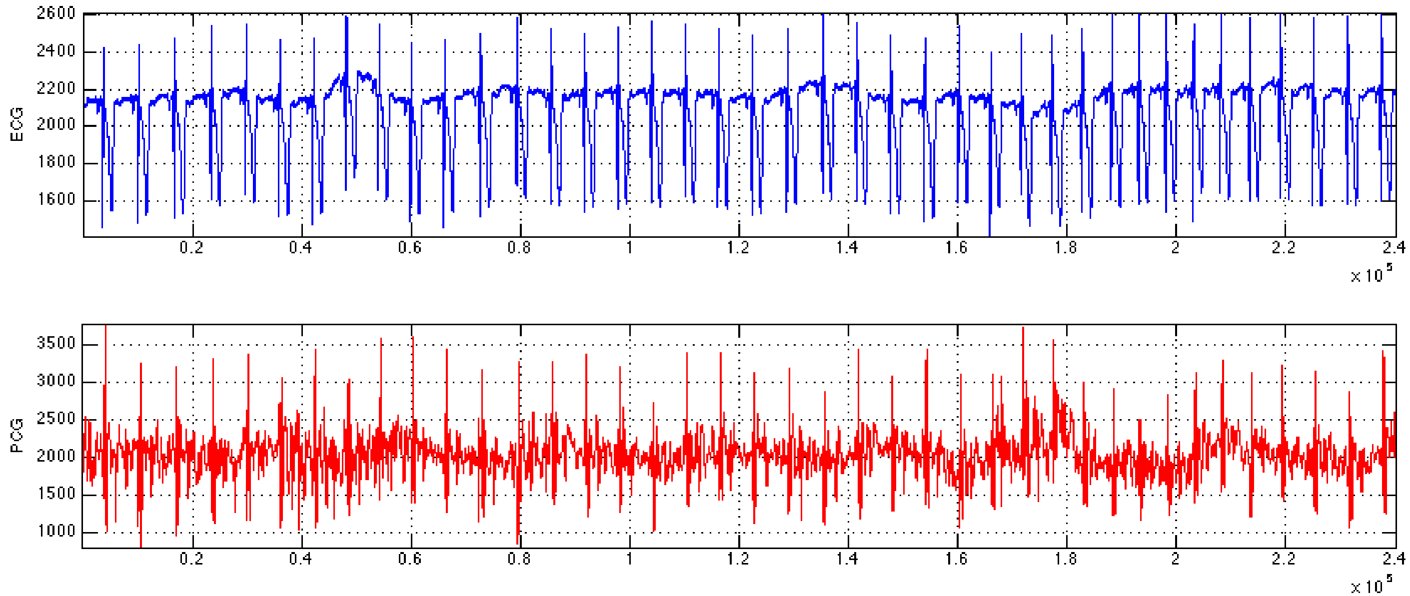
Multimodal signal/data fusion

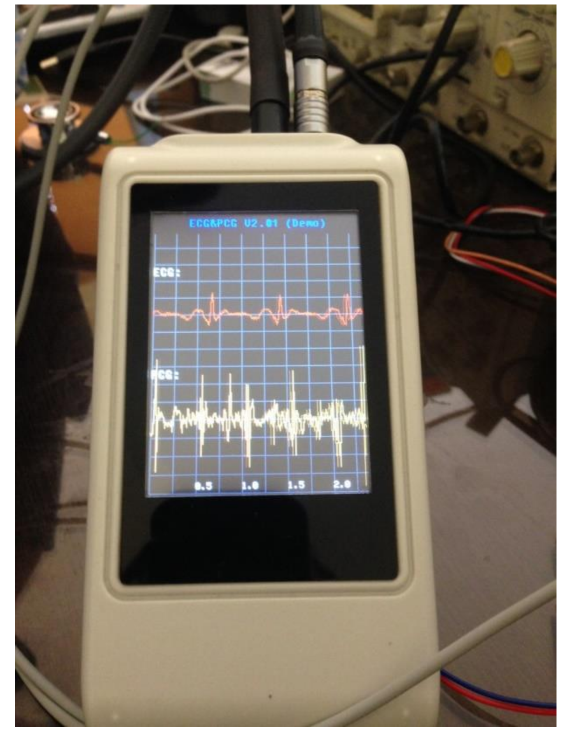
Multimodality

- Concept: The heart (as an electrophysiological organ)
- Parameters of interest: Heart rate, QT-intervals, ST-segment, T/R ratios, electromechanical features, S_1 and S_2 heart sounds and murmurs, etc.
- Modalities: ECG, PCG, Doppler, MCG, Cardiovascular magnetic resonance imaging (CMR), etc.



Multimodal ECG-PCG Analysis





VAP Inc. ECG-PCG device
(image subject to Copyright)

- Database: Simultaneous ECG and PCG database with 50 adult subjects during physical activity
- Findings: Meaningful differences between the heartrate parameters extracted from the ECG and the PCG during rest, walking, and sports.

Ref:
- Arsalan Kazemnejad (2018), Simultaneous electrocardiogram and phonocardiogram acquisition and analysis, Master’s thesis, Shiraz University.
- Samieinasab, M., & Sameni, R. (2015, May). Fetal phonocardiogram extraction using single channel blind source separation. In Electrical Engineering (ICEE), 2015 23rd Iranian Conference on (pp. 78-83). IEEE.
- Shiraz University Fetal Heart Sounds Database (SUFHSDB), Physionet. Available Online: https://physionet.org/physiobank/database/sufhsdb/

Theoretical Challenges in Multimodal Analysis

Fact: The information capacity of noisy channels/modalities are bounded
Challenge: Selection vs fusion between modalities; when and how?

Stereotypical example: Consider various noisy linear observations from a common source:

$$\mathbf{x}_1 = \mathbf{A}\cdot\mathbf{s} + \mathbf{n}_1\ ,\ \mathbf{x}_2 = \mathbf{B}\cdot\mathbf{s} + \mathbf{n}_2,\ \mathbf{x}_3 = \mathbf{C}\cdot\mathbf{s} + \mathbf{n}_3,\ \ldots$$

Question: For the "optimal" estimation of **s**, which is best:

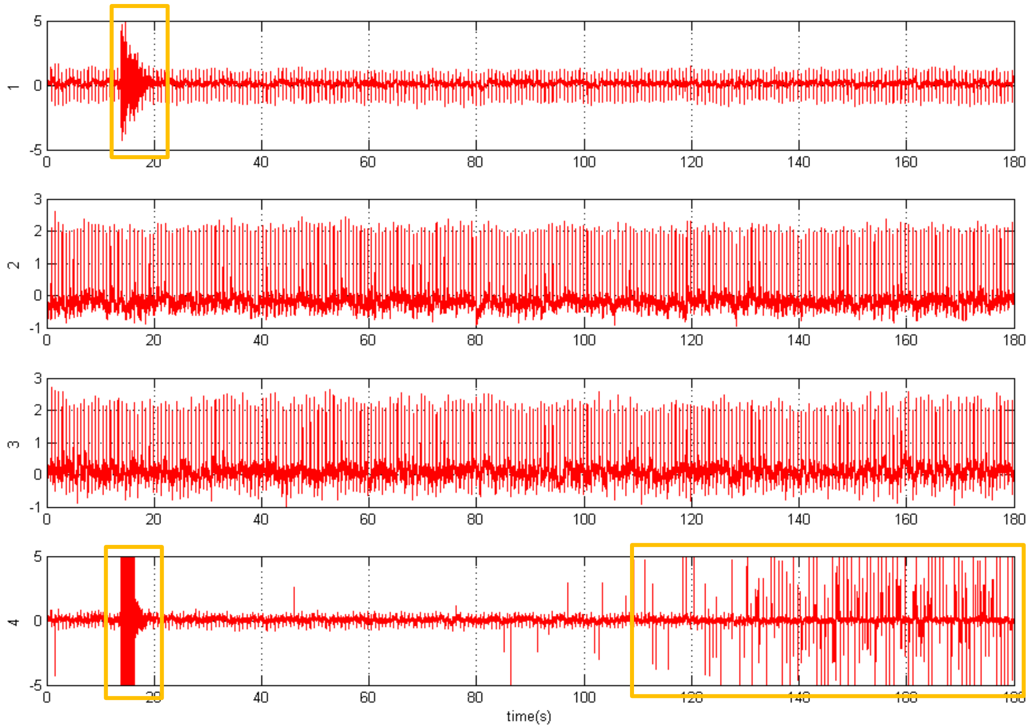
1) Select between the observations?
2) Fuse all observations as $[\mathbf{x}_1, \mathbf{x}_2, \mathbf{x}_3]$?
3) Use subsets: $\mathbf{x}_1$, $\mathbf{x}_2$, $\mathbf{x}_3$, $[\mathbf{x}_1, \mathbf{x}_2]$, $[\mathbf{x}_2, \mathbf{x}_3]$, etc.

Answer: From the estimation and information theoretical viewpoints (Cramér–Rao Lower Bound & Mutual Information), the answer is not trivial, even for the simplest linear data model and Gaussian noise

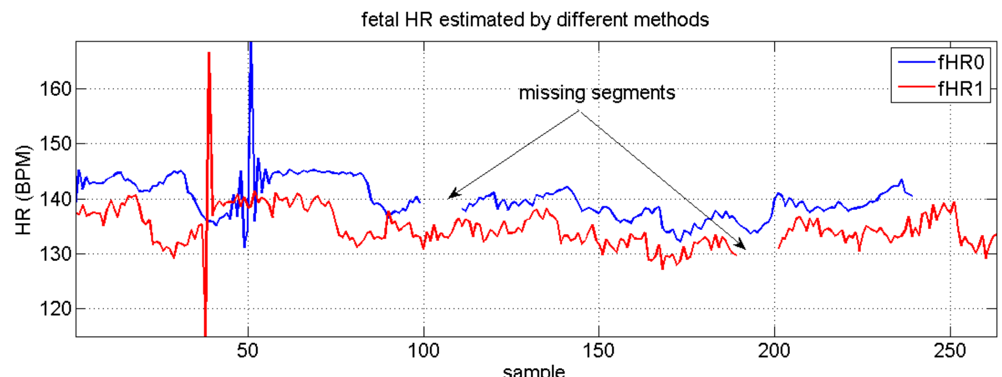
Our current research in GIPSA-lab: *To develop– and extend previous research– using an estimation and information theoretical framework for linear and nonlinear noisy multichannel/multimodal scenarios* (Chlaily et al, 2018)

Multimodality in Fetal Cardiography

Example: Multichannel fetal ECG and heart rate time series



Missing (or noisy) segment recovery



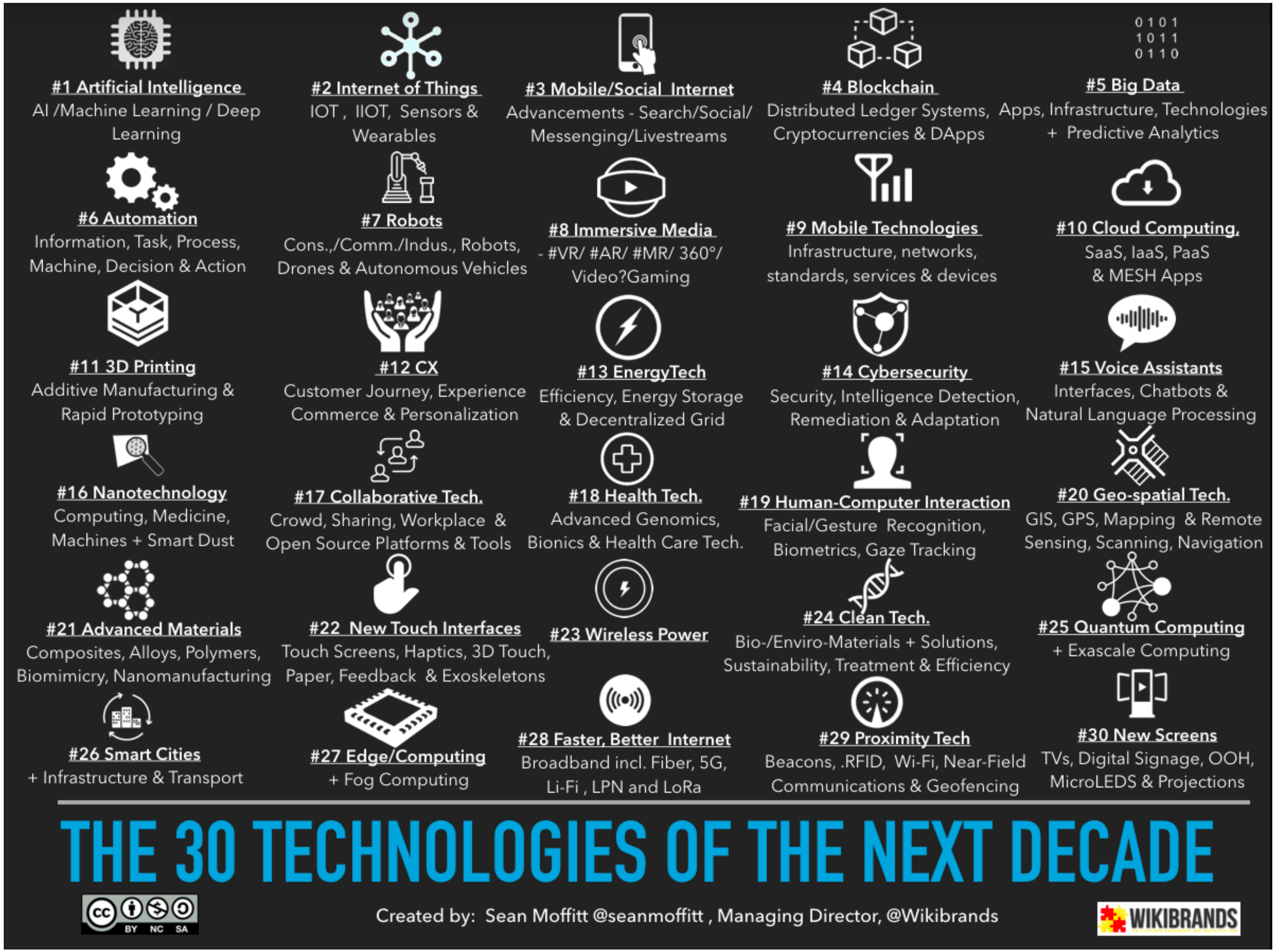
Misaligned/missing segments/noisy

Roadmap: To use dynamic models for segment/modality recovery, based on the innovation process (Sameni 2019), versus manifold techniques for partially missing data segment recovery (Rodrigues et al, 2018)

Perspectives

Technology trends

Technologies of the Next Decade



Insights

- Technologies and concepts that will continue to change biomedical engineering and prenatal care:

Mobile Internet	**Artificial Intelligence**	**Internet of Things**	**Big Data**	**Cloud Processing**
Blockchain	**Ultra-low and wireless -power electronics**	**Social Networks**	**Open-source software and hardware**	**Implementation-aware algorithm design**
?	**Virtual and Augmented Reality**	**Multimodality**	**Personalization**	**Beyond Bayesian**

The current Emory University BMI Department is the right time and place for such technology developments!

Thank you for your attention!