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(54) Title: PERIODIC ARTIFACT REDUCTION FROM BIOMEDICAL SIGNALS

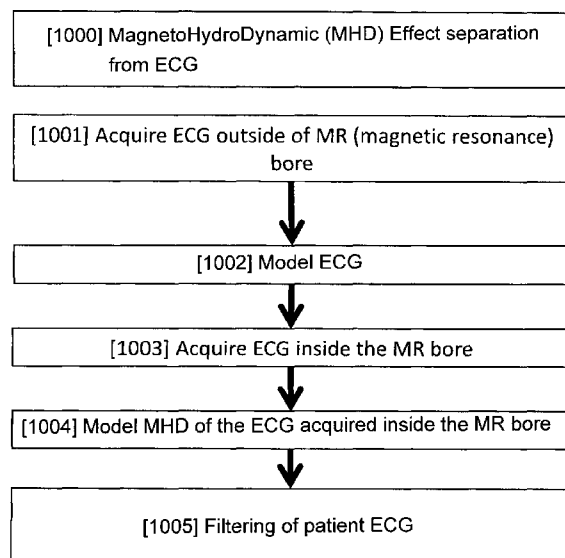


FIG. 1

(57) Abstract: The present disclosure provides systems and methods for separating periodic or pseudo periodic artifacts (e.g., magnetohydrodynamic (MHD) effects) from biomedical signals of interest (e.g., electrocardiograms (ECG)) by model-based nonlinear Bayesian filtering or other adaptive processes.



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PERIODIC ARTIFACT REDUCTION FROM BIOMEDICAL SIGNALS**CROSS-REFERENCE TO RELATED APPLICATION**

- [0001] This application claims priority to co-pending U.S. provisional application entitled "MAGNETOHYDRODYNAMIC EFFECT SEPARATION FROM ELECTROCARDIOGRAM" having serial no. 61/543,925, filed October 6, 2011, the entirety of which is hereby incorporated by reference as if fully set forth herein.

CROSS-REFERENCE TO RELATED DOCUMENTS

- [0002] This application incorporates by reference the following papers as if they were fully set forth herein expressly in their entireties:
- [0003] (a) "MagnetoHydroDynamic Effect separation from ECG acquired during MRI by using nonlinear Bayesian filtering" (attached hereto as Appendix A);
- [0004] (b) "Comparison of three artificial models of the MHD Effect on the Electrocardiogram" (attached hereto as Appendix B);
- [0005] (c) a poster presentation describing the separation of MHD effects from ECG data (attached hereto as Appendix C);
- [0006] (d) "Tracking arrhythmias in the ECG using a switching Kalman filter" (attached hereto as Appendix D);
- [0007] (e) J. Oster, R. Linares, Z. Tse, E. J. Schmidt and G. D. Clifford, "Realistic MHD modeling based on MRI blood flow measurements." In Proceedings of the annual meeting of the Int. Soc. for Magn. Res. in Med., 2012;
- [0008] (f) G. D. Clifford *et al.*, An artificial vector model for generating abnormal electrocardiographic rhythms. *Phys. Meas.*, 31:595-609, 2010;

- [0009] (g) R. Sameni, M. B. Shamsollahi, C. Jutten, and G. D. Clifford, "A Nonlinear Bayesian Filtering Framework for ECG Denoising." *IEEE Trans. Biomed. Eng.*, vol. 54, pp. 2172-2185, 2007;
- [0010] (h) O. Sayadi, M Shamsollahi and G. Clifford, "Robust detection of premature ventricular contractions using a wave-based Bayesian framework." *IEEE Trans. Biomed. Eng.*, vol. 57, no. 2, pp. 353-362, 2010; and
- [0011] (i) U.S. Patent Application No. 11/470,506, published as US2007/0260151 on November 8, 2007, by Clifford, filed on September 6, 2006, and having the title "Method and Device for Filtering, Segmenting, Compressing, and Classifying Oscillatory Signals" (hereafter "the Clifford Application") which is also incorporated by reference as if expressly set forth herein in its entirety.

FIELD OF THE DISCLOSURE

- [0012] The present disclosure relates generally to signal processing and, more particularly, to systems and methods for separating artifacts from acquired signals.

BACKGROUND

- [0013] Electrocardiograms (ECG) are often used in conjunction with magnetic resonance imaging (MRI) techniques. For example, ECG signals can be used to monitor a patient's physiological parameters during an MRI scan. Additionally, ECG signals can be used to synchronize MRI signal acquisition with heart motion.

[0014] The ECG signal, however, can be distorted because of various effects associated with the MRI. Thus, there exists a need in the industry for improved signal processing techniques.

SUMMARY

[0015] The present disclosure provides systems and methods for reducing or separating periodic (or semi-periodic) artifacts from biomedical signals acquired in noisy environments, such as during magnetic resonance imaging (MRI). Examples of artifacts that can be reduced or separated from such an acquired biomedical signal include magnetohydrodynamic (MHD) effects, ballistocardiogram effects and during fetal monitoring. Examples of the biomedical signals include electrocardiograms (ECG), electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), fetal ECG, blood pressure waveform and photoplethysmogram (PPG). Thus, for example, in various embodiments the present disclosure provides systems and methods for reducing or separating artifacts such as magnetohydrodynamic (MHD) effects from electrocardiograms acquired during a magnetic resonance imaging (MRI) examination. In other embodiments, for example, ballistocardiogram effects can be reduced or separated from electroencephalogram (EEG) acquisitions during functional MRI (fMRI).

[0016] In various embodiments, the reduction or separation of an artifact is accomplished by an adaptive filtering process, such as by nonlinear Bayesian filtering or other adaptive processes.

[0017] In an embodiment of the present disclosure, a method is provided for reducing or separating an artifact from a biomedical signal acquired in a noisy environment. The artifact can be periodic or semi-periodic. The method can include: acquiring a first biomedical signal apart from the noisy environment; modeling the first biomedical signal; acquiring a second biomedical signal of the same type but acquired in the noisy environment, the second biomedical signal including the artifact; modeling the second biomedical signal; and filtering the biomedical signal by determining an estimated signal from a combination of the modeled first and second biomedical signals and then separating the estimated combination of the first and second biomedical signals into an estimated first biomedical signal and an estimated second biomedical signal. The method can be a computer implemented method.

[0018] In an embodiment, a system is provided for reducing an artifact from a biomedical signal acquired in a noisy environment. The artifact can be periodic or semi-periodic. The system can include: a data acquisition system configured to acquire a first biomedical signal apart from the noisy environment, and to acquire a second biomedical signal of the same type but acquired in the noisy environment, the second biomedical signal including the artifact; and a processing system coupled to the data acquisition system, the processing system being configured to model the first biomedical signal, to model the second biomedical signal, and to filter the biomedical signal by determining an estimated signal from a combination of the modeled first and second biomedical signals and then separating the estimated combination of the first and second biomedical signals into an estimated first biomedical signal and an estimated second biomedical signal.

- [0019] In any one or more aspects, the system can be a computer system. The processing system can include: a local interface; and a processor, memory, a user interface, and an I/O device, each coupled to the local interface. The processing system can include a mobile application for a mobile device. The data acquisition system and the processing system can be integrated into a single device, or residing on separate devices.
- [0020] In an embodiment, a computer readable medium executable on a computer is provided for at least one of filtering, segmenting or classifying a biomedical signal including an artifact acquired in a noisy environment. The computer readable medium can execute the steps of: acquiring a first biomedical signal apart from the noisy environment; modeling the first biomedical signal; acquiring a second biomedical signal of the same type but acquired in the noisy environment, the second biomedical signal including the artifact; modeling the second biomedical signal; and filtering the biomedical signal by determining an estimated signal from a combination of the modeled first and second biomedical signals and then separating the estimated combination of the first and second biomedical signals into an estimated first biomedical signal and an estimated second biomedical signal.
- [0021] In any one or more aspects of the embodiments, the biomedical signal can be selected from one or more of an electrocardiogram (ECG), electroencephalogram (EEG), electromyogram (EMG), fetal ECG, blood pressure waveform or photoplethysmograph (PPG). The noisy environment can be a magnetic resonance imaging (MRI) scanner and the first biomedical signal can be acquired outside of the bore of the MRI scanner and the second biomedical signal can be acquired inside the

bore of the MRI scanner. The first and second biomedical signals can be each modeled as a pseudo periodic signal. The first and second biomedical signals can be modeled by fitting Gaussian parameters to the biomedical signals. The second biomedical signal can be modeled as a pseudo periodical signal with a periodicity being the same as the first biomedical signal or having a different periodicity. The cycle of the second biomedical signal can be approximated by a sum of Gaussians. The second biomedical signal can be modeled by solving Navier Stokes equations for different sections of an aortic arch of a subject and by propagating the resulting current source to the torso of the subject. The second biomedical signal can be modeled in accordance with a polynomial function, a spline function or a function like $f(t) = A \exp(-B(t-T_k)) \sin(2 \pi (t-T_k)/(T_{k+1} - T_k))$, T_k being the time of the k th R peaks and $T_k < t < T_{k+1}$ and A B being the parameters of this model. The method can further include the step of tracking the estimated first and second biomedical signals for abnormalities in the biomedical signal appearing as deviations from the estimated signals.

[0022] In any one or more aspects of the embodiments, the filtering can involve non-linear Bayesian filtering. The filtering can include Kalman filtering, particle filtering or Gaussian processes. The filtering step can include use of the following observation equations to provide an estimation of a periodic artifact to be reduced or separated from the biomedical signal:

$$\begin{cases} \varphi_k = \theta_k + v_{1,k} \\ s_k = P_k + QRS_k + T_k + MHD_k + v_{2,k} \\ s_k = MHD_k + \sum_i \alpha_i^{ECG} \exp\left(-\frac{\Delta\theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) + v_{3,k} \end{cases} \quad (3)$$

[0023] In any one or more aspects of the embodiments, the filtering can involve use of signal quality indices (SQI's) to automatically adjust the observation covariance noise matrix for Bayesian filtering. The filtering can involve use of a multiple model approach and a switching Kalman Filter to allow estimation of the different parameters for the models and selection of the best model.

[0024] In any one or more aspects of the embodiments, the artifact can be a magnetohydrodynamic (MHD) effect from an electrocardiogram (ECG) signal acquiring during a magnetic resonance imaging (MRI) technique and the first biomedical signal acquired can be an ECG, the second biomedical signal acquired can also be ECG, the modeling of the second biomedical signal can include modeling for MHD effect, and the filtering can include determining an estimated signal from the combination of the modeled first ECG signal and the modeled second ECG signal modeled for MHD effect and then separating the estimated combination of the first and second ECG signals into an estimated ECG signal and an estimated MHD signal.

[0025] Other systems, devices, methods, features, and advantages will be or become apparent to one with skill in the art upon examination of the following drawings and detailed description. It is intended that all such additional systems, methods, features,

and advantages be included within this description, be within the scope of the present disclosure, and be protected by the accompanying claims.

BRIEF DESCRIPTION OF THE DRAWINGS

- [0026] The patent or application file may contain at least one drawing executed in color. Copies of this patent or patent application publication with color drawings(s) will be provided by the Office upon request and payment of any necessary fee.
- [0027] Many aspects of the disclosure can be better understood with reference to the following drawings. The components in the drawings are not necessarily to scale, emphasis instead being placed upon clearly illustrating the principles of the present disclosure. Moreover, in the drawings, like reference numerals designate corresponding parts throughout the several views.
- [0028] FIG. 1 is a flowchart showing one embodiment of a process for separating magnetohydrodynamic (MHD) effects from an electrocardiogram (ECG).
- [0029] FIGS. 2A and 2B are flowcharts showing one embodiment of a process for Bayesian filtering of an acquired ECG signal.
- [0030] FIG. 3 is an example of ECG data obtained from a patient in the absence of a magnetic resonance imaging (MRI) magnetic field.
- [0031] FIG. 4 is an example of ECG data contaminated by MHD effects, obtained from a patient in the presence of a magnetic resonance imaging (MRI) magnetic field.
- [0032] FIG. 5 is an example of superimposed data, showing ECG data contaminated by MHD effects in a 1.5 Tesla (T) magnetic field, the MHD effects, and ECG data from which MHD effects are removed.

[0033] FIG. 6 is an example of superimposed data, showing ECG data contaminated by MHD effects in a 3.0 T magnetic field, the MHD effects, and ECG data from which MHD effects are removed.

[0034] FIG. 7 is a flow chart depicting an embodiment involving the use of signal quality indices (SQI's) to automatically adjust the observation noise covariance matrix for Bayesian filtering a biomedical signal

DETAILED DESCRIPTION OF THE EMBODIMENTS

[0035] Reference is now made in detail to the description of the embodiments as illustrated in the drawings. While several embodiments are described in connection with these drawings, there is no intent to limit the disclosure to the embodiment or embodiments disclosed herein. On the contrary, the intent is to cover all alternatives, modifications, and equivalents.

[0036] The various embodiments of the present systems and methods are directed to removing periodic (or semi-periodic) artifacts from biomedical signals of interest. As a non-limiting example, attention is first turned to an embodiment for removing (magnetohydrodynamic) MHD effects from electrocardiogram (ECG) signals acquired from a magnetic resonance imaging (MRI) examination, as shown in FIGS. 1 and 2. As described elsewhere herein other artifact effects can be separated from a biomedical signal of interest acquired in another noisy environment.

[0037] Electrocardiograms are important physiological signals used in diagnosing cardiovascular pathologies. ECGs are electrical recordings resulting from successive depolarization of cardiac cells. Magnetic resonance imaging is a non-invasive

radiological technique that allows for depiction of soft tissue and organs of the body. Using MRI it is possible to distinguish pathological tissue from healthy tissue, often without using a contrast agent.

[0038] Sometimes, physiological parameters, such as the ECG, are monitored in patients undergoing an MRI. ECGs are often used to detect cardiac abnormalities. Additionally, acquisition of an ECG during an MRI scan allows for synchronization of MRI acquisition with heart motion, which accounts for organ motion during the scan.

[0039] ECG relies on electromagnetic fields naturally induced by the body. The MRI environment has three major physical characteristics, which affect the ECG signal: high static magnetic field; fast varying magnetic fields (gradients); and radio frequency (RF) pulses. RF pulses induce an electrical field inside the body that can also interfere with the electrical components involved in measuring the ECG signal. Gradients induce electrical fields inside the body whose frequency range overlaps an ECG signal causing ECG signal distortion.

[0040] In addition to these distortions, the presence of the high static magnetic field in MRI scanners induces another, somewhat-indirect artifact on the ECG signal. This indirect effect, called the magnetohydrodynamic effect, or the Hall effect, arises from blood carrying electrically charged particles, such as iron, whose motion inside a magnetic field creates a current source. The strength of the MRI magnetic field is such that the current source created by the blood flow is about the same magnitude as that of the heart natural electrical activity. It has been shown that the main contribution of the MHD effect is induced by the blood ejection through the aortic

arch, because of the geometry of the arch, the diameter of the artery and the blood velocity. Given the timing and the amplitude of this phenomenon, the ST to T wave segment of the ECG is hidden behind a high level of noise and the detection of pathological ventricular repolarization is currently impossible during MRI. This is becoming a growing concern with the development of applications such as very high field cardiac imaging, MR guided surgery, cardiac imaging during exercise stress, or intra-cardiac electrophysiology guided by real-time MRI. The electromagnetic field associated with this current source affects the acquired ECG signal, potentially masking cardiac abnormalities. As a result, it becomes useful to separate the MHD effect from the ECG signal to allow for a more accurate representation of the ECG, and correspondingly a more accurate diagnosis of cardiac abnormalities, should such abnormalities exist.

[0041] Various embodiments of the present disclosure, therefore, provide systems and methods for removing contaminants from a time series that is similar in frequency, morphology, amplitude, and timing to the signal of interest. Due to the contaminant's similarity to the signal of interest, these types of contaminants are difficult to remove. Currently existing techniques employ simple template matching (and subtraction) or simple adaptive filtering. However, in the case of template subtraction, the changing morphology and timing of the beat is not modeled well. So, residual errors cause clinically significant distortions in the electrocardiogram. Adaptive filtering carries little understanding of either the signal of interest or the contaminant signal. Thus, adaptive filtering techniques *per se* may not be ideal.

[0042] Various embodiments of the present systems and methods combine a model of both the artifact and the signal of interest, which adapts to sample-by-sample changing dynamics to make estimates of underlying sources of information. Thus, for example, embodiments described herein use models of both a biomedical signal of interest, such as ECG, and artifact sources from the individual whose physiological parameters are being measured. Thus, the resulting signal is custom tailored to each individual.

[0043] In various embodiments, the separation of the two contributions (for example, ECG and artifact) relies on prior knowledge of the uncontaminated ECG and a model of the artifact. Thus, in any one or more aspects, an ECG signal acquired inside an MR bore can be approximated or modeled by the superposition of an ECG signal acquired without artifact (i.e., without MHD effect) and of an MHD signal. The disclosed systems and methods can also take into account the non-stationary nature of the signals, thereby allowing the parameters of the models to evolve over time. This allows for accurate patient monitoring.

[0044] Specifically, FIG. 1 is a flowchart showing an embodiment of a process (1000) for separating MHD effects from an ECG acquired during an MRI examination. As shown in FIG. 1, the process comprises the steps of acquiring (1001) an ECG from a patient outside of the bore of the magnetic resonance imaging (MRI) scanner. An example of ECG data that has been acquired from outside of the bore is shown in FIG. 3.

[0045] Thereafter, the ECG is modeled (1002). As an example the ECG can be modeled by fitting Gaussian parameters to the ECG. In an aspect, the Gaussian

parameters can be fit to the ECG using the methods described in the aforementioned Clifford Application (US published application no. US 2007/026015), which is incorporated by reference as if expressly set forth herein in its entirety. The ECG signal can be modeled as a pseudo periodic signal, whose period cycle is a sum of Gaussians, such that:

$$\begin{cases} \theta_k = (\theta_{k-1} + \omega\delta) \bmod 2\pi \\ z_k = -\sum_i \delta \frac{\alpha_i \omega}{b_i^2} \Delta\theta_{i,k-1} \exp\left(-\frac{\Delta\theta_{i,k-1}^2}{2b_i^2}\right) + z_{k-1} + \eta \end{cases} \quad (1)$$

where θ_k is the angular position in cylindrical coordinates, $\omega = 2\pi/RR$ the angular speed with δ being the sampling period and RR being the time between adjacent heart beats. z_k represents the ECG value in mV at time k . α_i is the amplitude of the i^{th} Gaussian, b_i is the width of the i^{th} Gaussian, and $\Delta\theta_{i,k-1} = (\theta_{k-1} - \xi_i) \bmod 2\pi$, with ξ_i being the angular position of the i^{th} Gaussian.

[0046] In another aspect, the ECG can be modeled with a dynamical vector cardiograph (VCG) model, that represents each of the three axes of the VCG by a sum of Gaussians and then applies a Dower transform. See, e.g., G. D. Clifford *et al.*, An artificial vector model for generating abnormal electrocardiographic rhythms. *Phys. Meas.*, 31:595-609, 2010. In order to model a pathological ventricular repolarization, the parameters of the Gaussian representing the T wave can be evolving. The T wave inversion can be modeled by inverting the amplitude of the T wave Gaussians with a logistic function over ten cycles. The prolonged QT interval

can be modeled by moving forward angular position of the T wave Gaussians with a logistic function over 10 cycles with an amplitude of $0.1rad$.

[0047] Upon modeling (1002) the ECG, another ECG is acquired (1003) from the patient from inside of the bore of the MRI scanner. An example of ECG data that has been acquired from inside of the bore is shown in FIG. 4. As shown in FIG. 4, the ECG data exhibits contamination from MHD effects.

[0048] Thereafter, an MHD effect is modeled (1004). For example the MHD effect can be modeled as a pseudo periodical signal with periodicity being the same as the ECG signal, though its periodicity need not be the same as the ECG signal. In an aspect the model of the MHD effect can be computed by solving the Navier Stokes equations for different sections of the aortic arch (which has been shown to be the main contributor of the artifact) and by propagating the resulting current source to the torso. For example, the MHD effect can be modeled by using 4D blood flow measurements from a phase contrast MRI technique. The blood flow can be measured in sections of the aortic arch (such as 4 sections). 3D models of the aortic arch and the human torso can be used to project the current source onto the torso for computing the biopotential on the torso at the different electrode positions. See, e.g., J. Oster, R. Linares, Z. Tse, E. J. Schmidt and G. D. Clifford, "Realistic MHD modeling based on MRI blood flow measurements." In Proceedings of the annual meeting of the Int. Soc. for Magn. Res. in Med., 2012. See also, for example, the poster presentation, Appendix C hereto. In various embodiments, the MHD periodicity can be approximated by fitting model parameters, for example a sum of Gaussians. The number of Gaussians can vary between the subjects as the effect is

strongly influenced by blood flow characteristics. For example, the blood flow can be more or less laminar, and the presence of vortices induces the presence of high frequencies on the MHD effect and increases the number of Gaussians required for its approximation.

[0049] It should be appreciated that, for other embodiments, the MHD effect can also be modeled in accordance with the methods set forth in Appendix B hereto, "Comparison of three artificial models of the MHD Effect on the Electrocardiogram." These methods also include polynomial functions, spline functions or functions like $f(t) = A \exp(-B(t-T_k)) \sin(2 \pi (t-T_k)/(T_{k+1} - T_k))$, T_k being the time of the k^{th} R peaks and $T_k < t < T_{k+1}$ and A B being the parameters of this model.

[0050] The out-of-bore ECG acquisition (1001), the ECG modeling (1002), the in-bore ECG acquisition (1003), and the MHD modeling (1004) can be seen as the initialization process, which is performed at the beginning of an MRI examination.

[0051] After the initialization process, the patient's ECG signal can be filtered. For example, the patient's ECG signal can be filtered using Bayesian filtering (1005) or other adaptive processes. Exemplary Bayesian filtering processes include the Kalman Filter (such as an Extended Kalman Filter), the particle filter and Gaussian processes. One embodiment of a Bayesian filtering (1005) process is shown in FIG. 2. Bayesian filtering aims at recursively estimating a set of hidden variables, x , given a sequence of noisy observation, y . The observations are related to the hidden state (the artifact to be removed) by a supposedly known observation equation and the evolution state can be determined by the evolution equation, described in more detail below.

[0052] As shown in FIGs. 2A and 2B, one embodiment of a Bayesian filtering (1005) process begins with the inputting (2000) of data. This data includes patient ECG acquired (2005) during an MRI scan, the modeled (1002) ECG signal, and the modeled (1004) MHD signal. Given these inputs (2000), an estimated ECG+MHD signal is calculated (2001) from the acquired (2005) ECG, using the modeled (1002) ECG signal and the modeled (1004) MHD signals, respectively. The resulting output (2002) from the calculated (2001) ECG+MHD signals is then separated (2003) into an estimated ECG signal and an estimated MHD signal, which are subsequently outputted (2004). Results from such a Bayesian filtering (1005) process are shown in FIGS. 5 and 6, for field strengths of 1.5T and 3.0T, respectively.

[0053] In a non-limiting aspect, the ECG signal can be first recorded during installation of the patient, that is before entering the MRI bore. A number of cycles, for example 10 ECG cycles, can be recorded outside of the MRI bore and used in order to compute an ECG template and initialize Gaussian parameters by, for example, computing the Gaussian parameters of the mean ECG cycle. See, e.g., R. Sameni, M. B. Shamsollahi, C. Jutten, and G. D. Clifford, "A Nonlinear Bayesian Filtering Framework for ECG Denoising." *IEEE Trans. Biomed. Eng.*, vol. 54, pp. 2172-2185, 2007. Once the subject is inserted inside of the MRI bore, a number of cycles, for example 10 cycles, can be extracted and used to compute a mean template. This template corresponds to the sum of the ECG and MHD. An MHD template can be estimated by subtracting the ECG template. The MHD Gaussian parameters can then be initialized in the same way as for the ECG. A Bayesian filter, for example an Extended Kalman Filter (EKF), can then be applied for separating an estimated ECG

and an estimated MHD and denoising. See, e.g., O. Sayadi, M Shamsollahi and G. Clifford, "Robust detection of premature ventricular contractions using a wave-based Bayesian framework." *IEEE Trans. Biomed. Eng.*, vol. 57, no. 2, pp. 353-362, 2010.

[0054] By tracking the estimated ECG signal and the estimated MHD signal over time, abnormalities in the ECG, such as ischemia, will appear as deviations from the estimated signals. It should also be noted that cardiac output, ejection time, and ejection fraction, which are all useful clinical parameters, can be estimated with the resolution of the MHD. An example of simulating MHD effect from blood flow measurements is shown in Appendix B hereto, "Comparison of three artificial models of the MHD Effect on the Electrocardiogram."

[0055] During an MRI acquisition, the MHD effect overlaps the ECG signal in the frequency domain. In an exemplary embodiment, the Kalman Filter based technique can be used to separate MHD and ECG dynamics, since they are mathematically modeled. This approach takes into consideration that both ECG and MHD are non-stationary. Since the MHD contribution occurs simultaneously with the clinically important ECG waves, the separation of the dynamics is difficult, if its dynamics are not temporally separated. In an embodiment, to overcome this difficulty, a new observation equation is introduced in which a synthetic signal is created by subtracting from the raw ECG observation the prior information on the ECG signal (e.g., the sum of Gaussians of the ECG model given the synthetic phase signal). This new observation gives an approximation of the MHD effect.

[0056] The evolution equations can be written as follows:

$$\left\{ \begin{array}{l}
 \theta_k = (\theta_{k-1} + \omega\delta) \mod 2\pi \\
 P_k = -\sum_{i=1}^2 \delta \frac{\alpha_i^{ECG} \omega}{b_i^{ECG^2}} \Delta\theta_{i,k-1}^{ECG} \exp\left(-\frac{\Delta\theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) \\
 \quad + P_{k-1} + \eta_p \\
 QRS_k = -\sum_{i=3}^5 \delta \frac{\alpha_i^{ECG} \omega}{b_i^{ECG^2}} \Delta\theta_{i,k-1}^{ECG} \exp\left(-\frac{\Delta\theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) \\
 \quad + QRS_{k-1} + \eta_{QRS} \\
 T_k = -\sum_{i=6}^7 \delta \frac{\alpha_i^{ECG} \omega}{b_i^{ECG^2}} \Delta\theta_{i,k-1}^{ECG} \exp\left(-\frac{\Delta\theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) \\
 \quad + T_{k-1} + \eta_T \\
 MHD_k = -\sum_i \delta \frac{\alpha_i^{MHD} \omega}{b_i^{MHD^2}} \Delta\theta_{i,k-1}^{MHD} \exp\left(-\frac{\Delta\theta_{i,k-1}^{MHD^2}}{2b_i^{MHD^2}}\right) \\
 \quad + MHD_{k-1} + \eta_{MHD} \\
 \alpha_{i,k}^{ECG} = \alpha_{i,k-1}^{ECG} + \varepsilon_{\alpha,i} \\
 b_{i,k}^{ECG} = b_{i,k-1}^{ECG} + \varepsilon_{b,i} \\
 \xi_{i,k}^{ECG} = \xi_{i,k-1}^{ECG} + \varepsilon_{\xi,i}
 \end{array} \right. , \quad (2)$$

[0057] The observation equations are given by:

$$\left\{ \begin{array}{l}
 \varphi_k = \theta_k + v_{1,k} \\
 s_k = P_k + QRS_k + T_k + MHD_k + v_{2,k} \\
 s_k = MHD_k + \sum_i \alpha_i^{ECG} \exp\left(-\frac{\Delta\theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) + v_{3,k}
 \end{array} \right. . \quad (3)$$

[0058] These evolution equations account for the evolution of the ECG signal over time by estimating the parameters of the Gaussians that represent the ECG signal.

The evolution equations, Eq. (2), and the observation equations, Eq. (3), are explained

in greater detail in Appendix A hereto, "MagnetoHydroDynamic Effect separation from ECG acquired during MRI by using nonlinear Bayesian filtering," which shows experimental data using the methods described herein.

[0059] In this embodiment, for the evolution equation for the MHD contribution, the Gaussian parameters are not included even though the signal is non-stationary, however the uncertainty in the noise allows its consideration in this model.

[0060] Bayesian filtering techniques rely on some parameter adjustments. Their initialization should be done such that they reflect properly the problem encountered. The observation noise covariance matrix of the Bayesian filter reflects the level of trust in the measurements. In the case where the measurements are biomedical signal acquisitions, which are non-stationary, the level of trust in the measurements can vary dramatically during an examination given patient motion and other external factors. In an aspect, signal quality indices (SQI's) can be used to adjust automatically the observation noise covariance matrix for optimal Bayesian filtering. As a non-limiting example, when using an Extended Kalman Filter (EKF) the observation and evolution equations can be linearized as:

$$\begin{cases} \underline{x}_{k+1} = f(\underline{x}_k, \underline{w}_k, k) \\ \quad \approx f(\hat{\underline{x}}_k, \hat{\underline{w}}_k, k) + A_k(\underline{x}_k - \hat{\underline{x}}_k) + B_k(\underline{w}_k - \hat{\underline{w}}_k) \\ \underline{y}_k = g(\underline{x}_k, \underline{v}_k, k) \\ \quad \approx g(\hat{\underline{x}}_k, \hat{\underline{v}}_k, k) + M_k(\underline{x}_k - \hat{\underline{x}}_k) + N_k(\underline{v}_k - \hat{\underline{v}}_k) \end{cases}$$

with

$$\begin{aligned} A_k &= \left. \frac{\partial f(\underline{x}, \underline{w}_k, k)}{\partial \underline{x}} \right|_{\underline{x}=\hat{\underline{x}}_k} & B_k &= \left. \frac{\partial f(\hat{\underline{x}}_k, \underline{w}, k)}{\partial \underline{w}} \right|_{\underline{w}=\hat{\underline{w}}_k} \\ M_k &= \left. \frac{\partial g(\underline{x}, \underline{v}_k, k)}{\partial \underline{x}} \right|_{\underline{x}=\hat{\underline{x}}_k} & N_k &= \left. \frac{\partial g(\hat{\underline{x}}_k, \underline{v}, k)}{\partial \underline{v}} \right|_{\underline{v}=\hat{\underline{v}}_k} \end{aligned} \quad (4)$$

We can then apply standard Kalman equations:

$$\begin{cases} \hat{\underline{x}}_k^- = f(\hat{\underline{x}}_{k-1}^+, \underline{w}, k) \Big|_{\underline{w}=\underline{0}} \\ H_k^- = A_{k-1} H_{k-1}^+ A_{k-1}' + B_{k-1} Q_{k-1} B_{k-1}', \\ \hat{\underline{x}}_k^+ = \hat{\underline{x}}_k^- + K_k r_k \\ K_k = H_k^- M_k' [M_k H_k^- M_k' + N_k R_k N_k']^{-1} \\ r_k = \underline{y}_k - g(\hat{\underline{x}}_k^-, \underline{v}, k) \Big|_{\underline{v}=\underline{0}} \\ H_k^+ = H_k^- - K_k M_k H_k^- \end{cases} \quad (5)$$

$$\text{with } Q_k = E\{\underline{w}_k \underline{w}_k^T\} \text{ and } R_k = E\{\underline{v}_k \underline{v}_k^T\} \quad (6) \quad (7)$$

that are a function of time and that can be adjusted to an estimated noise level by use of a Signal Quality Index (SQI):

$$V_k = [V_{1,k} \ V_{2,k}]^T \quad (8)$$

Ideally the energy of $v_{2,k}$ is a linear function of SQI, $E\{v_{2,k}^2\} = \text{cte SQI}$, with cte being a constant.

Thus when running an Extended Kalman Filter with an adaptive observation noise covariance matrix, automatic adjustment or adaption can be done with amplification signal

$$R_k(2,2) = (SQI) R_0(2,2) \quad (9)$$

[0061] FIG. 7 is a flow chart that depicts an aspect of use of a Signal Quality Index to automatically adjust the observation noise covariance matrix to optimize Gaussian Filtering. An acquired biomedical signal is input (701) into the filtering scheme. A Signal Quality Index (SQI) can be computed and used to estimate a noise level (702) in the inputted biomedical signal. Meanwhile the biomedical signal can be analyzed (703) with a Gaussian Filtering technique, such as an Extended Kalman Filter (EKF). The observation noise covariance matrix of the filter can be adjusted (704) to the estimated noise level. For example, the adaption of the noise level can be done with the above amplification signal. This technique, thus, allows for optimal analysis of biomedical signals even when the conditions of recording are changing (and thus also the level of noise).

[0062] In addition, model-based Bayesian filtering techniques rely on the prior knowledge of a system. For example, in the aspect herein involving acquisition of ECG signals, this prior knowledge is the dynamics of the ECG signal represented in one aspect by a sum of Gaussians. The occurrence of pathological rhythms can be followed by a drastic change of the ECG morphology in which case the prior

knowledge will not correspond to the signal acquired in the noisy environment. In an aspect a multiple model approach, during which the best-fitted model will be automatically selected, can be employed for the analysis of such biomedical signals. For example, different models can reflect a normal case, a recurrent pathologic rhythm such as Premature Ventricular Rhythm, and an unexpected pathological rhythm or any abnormality which can be represented by a dummy model and can allow detection of abnormalities in the signal. In an aspect, a switching Kalman Filter can be used to allow estimation of the different model parameters and the selection of the best model in parallel. The best model can then be applied in the filtering step.

[0063] In an exemplary embodiment, in an aspect of acquiring ECG signals, the ECG signal acquired (1001) outside of the noisy environment can be modeled (1002) not just for a normal case, but also for example for Premature Ventricular Contraction (PVC) and for an X factor mode, i.e. and unknown beat (whether artifacts or unknown pathological beat). Thus, in this embodiment, the acquired ECG signal (1001) is modeled for not just one mode but for the three different modes. The types of modes and the number of modes modeled are not limited to these particular three modes. Instead any number and types of modes can be modeled. For each new ECG signal acquired inside the noisy environment the ECG is filtered. In the aspect of a Kalman filter, for each new ECG sample acquired from the noisy environment the Kalman filter is computed for each of the three modes and the likelihood is then used to choose which of the three modes is best suited to the observation. The switching Kalman filter is then allowed to switch to the most likely mode and filter (1005) the ECG signal using the most appropriate prior knowledge (i.e., the modeled signal

acquired outside of the noisy environment of the most likely of the three modes). An example of an application of a switching Kalman Filter is described in greater detail in Appendix D hereto, "Tracking arrhythmias in the ECG using a switching Kalman filter."

[0064] The processes of FIGS. 1 and 2, and their component steps, may be implemented in hardware, software, firmware, or a combination thereof. In the preferred embodiment(s), these processes are implemented in software or firmware that is stored in a memory and that is executed by a suitable instruction execution system. If implemented in hardware, as in an alternative embodiment, these processes can be implemented with any or a combination of the following technologies, which are all well known in the art: a discrete logic circuit(s) having logic gates for implementing logic functions upon data signals, an application specific integrated circuit (ASIC) having appropriate combinational logic gates, a programmable gate array(s) (PGA), a field programmable gate array (FPGA), etc.

[0065] Any process descriptions or blocks in flow charts should be understood as representing modules, segments, or portions of code which include one or more executable instructions for implementing specific logical functions or steps in the process, and alternate implementations are included within the scope of the preferred embodiment of the present disclosure in which functions may be executed out of order from that shown or discussed, including substantially concurrently or in reverse order, depending on the functionality involved, as would be understood by those reasonably skilled in the art of the present disclosure.

[0066] The processes of FIGS. 1 and 2 may be implemented as a computer program, which comprises an ordered listing of executable instructions for implementing logical functions, can be embodied in any computer-readable medium for use by or in connection with an instruction execution system, apparatus, or device, such as a computer-based system, processor-containing system, or other system that can fetch the instructions from the instruction execution system, apparatus, or device and execute the instructions. In the context of this document, a "computer-readable medium" can be any means that can contain, store, communicate, propagate, or transport the program for use by or in connection with the instruction execution system, apparatus, or device. The computer-readable medium can be, for example but not limited to, an electronic, magnetic, optical, electromagnetic, infrared, or semiconductor system, apparatus, device, or propagation medium. More specific examples (a nonexhaustive list) of the computer-readable medium would include the following: an electrical connection (electronic) having one or more wires, a portable computer diskette (magnetic), a random access memory (RAM) (electronic), a read-only memory (ROM) (electronic), an erasable programmable read-only memory (EPROM or Flash memory) (electronic), an optical fiber (optical), and a portable compact disc read-only memory (CDROM) (optical). Note that the computer-readable medium could even be paper or another suitable medium upon which the program is printed, as the program can be electronically captured via, for instance, optical scanning of the paper or other medium, then compiled, interpreted or otherwise processed in a suitable manner if necessary, and then stored in a computer memory.

[0067] Although exemplary embodiments have been shown and described, it will be clear to those of ordinary skill in the art that a number of changes, modifications, or alterations to the disclosure as described may be made. For example, while one specific embodiment of removing MRI-related artifacts from ECG signals is described in detail, this disclosure can more broadly be seen as teaching systems and methods for reducing periodic artifacts from biomedical signals, and even more broadly as removing noise on any oscillatory signal for which an approximate model can be constructed, whether as sums of Gaussians or otherwise. Thus, for example, the disclosed systems and methods can be used to remove ballistocardiogram effects from electroencephalogram (EEG) acquisitions during functional MRI (fMRI), or any other bioelectric signals acquired during MRI (e.g., electrooculogram (EOG), electromyogram (EMG), fetal ECG, etc).

[0068] All such changes, modifications, and alterations should therefore be seen as within the scope of the disclosure.

Appendix A

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MagnetoHydroDynamic Effect separation from ECG acquired during MRI by using nonlinear bayesian filtering

Julien Oster, Gari Clifford, *Senior Member, IEEE*,**Abstract**—The abstract goes here.**Index Terms**—MagnetoHydrodynamic, Electrocardiogram, Bayesian filtering.

I. INTRODUCTION

ELECTROCARDIOGRAM (ECG) is one if not the most important physiological signal for the diagnosis of cardiovascular pathologies. It is the electrical recording resulting from the successive depolarisation of cardiac cells. This signal has been studied over more than a century and many advanced signal processing techniques have been developed for a wide range of applications [1]. One can for example cite the detection of ischemia of the myocardium by detecting a low voltage feature on the ECG, the elevation of the ST segment.

Magnetic Resonance Imaging (MRI) is a recently developed non-invasive radiological technique, whose field of applications is constantly growing. This technique allows us to depict soft tissue and has been applied to all organs and parts of the body. The discrimination of pathological from healthy tissue has made possible without ionising the patient and usually without injecting contrast agents.

These techniques, apparently completely independent, are linked for two major reasons. Firstly, during the whole MRI procedure the patient has to be taken care of and his state should not be deteriorating. A patient monitoring has thus to be performed, and several physiological parameters have thus to be followed [2]. Among all the physiological parameters required, the ECG signal is one of the most important due to its ability to detect any cardiovascular abnormality. Secondly, the MRI is a rather slow imaging technique and acquisition of an image lasts several seconds and consists of a succession of Nuclear Magnetic Resonance (NMR) experiments. When the organ depicted is moving periodically, as for example the heart, the successive experiments have to be performed while the organ is at the exact same position. The use of ECG signal is the clinical standard in order to synchronise MRI acquisition with heart motion [3]. Each NMR experiment is triggered by the detection of the most characteristic feature of the ECG signal, that is the QRS complex. Another way of synchronisation is to reorder MRI acquisitions retrospectively given the detection of the QRS complexes.

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Both techniques rely on Electromagnetic fields, whether naturally induced by the body or specifically created to build an image, and thus these two techniques highly interfere one on each other. MRI environment consists of three major physical characteristics (high static magnetic field, fast varying magnetic fields (gradients), RadioFrequency (RF) pulses), each of them are adding a significant contribution on the ECG signal. RF pulses induce some electrical field inside the body, but can also interfere with the electronic components and the wires can be antennas and also cause heat hazards. Gradients induce electrical fields inside the body whose frequency range overlaps ECG signal and thus is highly distorting. The presence of the high static magnetic field induces another artefact on the ECG signal, but indirectly. The blood is carrying some electrically charged particles, whose motion inside a magnetic field is creating a current source, this effect has been called MagnetoHydroDynamic (MHD) effect or Hall effect [4]. This creation occurs for every standard ECG acquisitions, since the earth magnetic field is always present. However the strength of the MRI magnetic field is such that the current source created by the blood flow is about the same magnitude than the heart natural electrical activity. It has been shown that the main contribution of the MHD effect is induced by the blood ejection through the aortic arch, due to geometry of the arch, diameter of the artery and its blood velocity [5], [6]. Some studies have been carried to build some realistic models of the MHD effect superposition onto the ECG signal [5], [7]. RF pulse artefacts have been tackled by the design of specific ECG sensor hardware (Faraday cage, optical wire, analog filtering...) [8]–[10]. Several signal processing techniques have been proposed for the suppression of gradient artefacts ranging from wavelets [11], [12], impulse response modelling with off-line estimation [13], [14], adaptive filtering [15] or nonlinear bayesian filtering [16] and independent component analysis [17]. However the separation of the MHD effect from the ECG signal has not been investigated intensively, certainly due to the high complexity of this problem. Indeed, it consists in the separation of two highly dependent signals, blood flow being in aorta being the consequence of the heart contraction induced by the depolarisation of its cells. These two sources are originating in very close locations and last but not least this problem is non stationary. By taking that into account, one can consider that methods that are popular for the blind source separation problem such as independent component analysis (ICA) [18] or periodic component analysis (PiCA) [19] will fail to extract MHD effect from the ECG signal.

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First class of methods trying to tackle the MHD effect problem only consists in the detection of QRS complexes by discarding detections of the MHD effect, whether with a priori knowledge of the QRS complexes orientation [20] or by use of wavelets [12]. Second class of techniques consists in the extraction of the MHD effect. The few proposed method only rely on template extraction (whether ECG or MHD) and then simply consists in the suppression of the template of one signal to have an estimation of the other [21], [22]. Recently some adaptive technique, which overcomes some limitations of the previously mentioned methods, has been presented [23]–[26].

The lack of accurate method for extracting the MHD effect from the ECG signal is even more a limitation since a precise analysis of the ECG is furthermore required for many applications in growing fields. One can for example cite cardiac imaging in higher magnetic field scanner (3T or 7T) [27]–[29], MR guided surgery during which ischemia detection is mandatory [30]–[33] or cardiac imaging during exercise stress [34]–[36].

In the herein paper, we will propose to extend the use of an ECG model and nonlinear bayesian filtering to the separation of the MHD effect.

II. MATERIALS AND METHODS

A. Method

ECG signal has been recently modelled as pseudo periodic signal, whose period cycle was a sum of gaussians [37]. It has been shown that the use of seven gaussians, the two firsts representing the P wave, the three nexts representing the QRS complex and the two lasts the T wave [38].

$$\begin{cases} \theta_k = (\theta_{k-1} + \omega\delta) \bmod 2\pi \\ z_k = -\sum_i \delta \frac{\alpha_i \omega}{b_i^2} \Delta\theta_{i,k-1} \exp\left(-\frac{\Delta\theta_{i,k-1}^2}{2b_i^2}\right) + z_{k-1} + \eta \end{cases} \quad (1)$$

where θ_k is the angular position in the cylindrical coordinates, $\omega = 2\pi/RR$ the angular speed, δ being the sampling period. z_k represents the ECG value in mV at time k ; and α_i, b_i, ξ_i being respectively the amplitude, width and angular position of the i^{th} gaussian, with $\Delta\theta_{i,k-1} = (\theta_{k-1} - \xi_i) \bmod 2\pi$.

A depiction of the representation in cylindrical coordinates and the approximation by gaussian functions is given in figure 1.

The ECG model can be approximated through the estimation of 21 parameters (three per gaussian), which can be performed online with nonlinear bayesian filtering [38]–[40]. This method offers the advantage of using the prior knowledge for accurate denoising but also the possibility of following its nonstationarity.

MHD effect can also be modelled as a pseudo periodical signal, the periodicity being exactly the same than the ECG signal. The periodic signal can also be approximated by a sum of gaussians, as for every signal, but the number of gaussians can vary between the subjects. The blood flow can be more or less laminar and the presence of vortices induces the presence

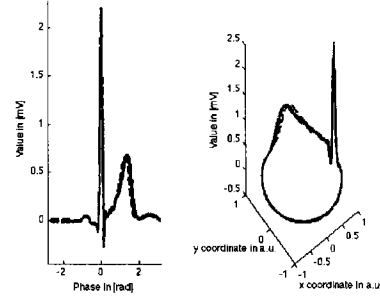


Fig. 1. ECG modelling. ECG signal in blue and its approximation by Gaussians functions in red.

of high frequencies on the MHD effect and increases the number of gaussians required for its approximation.

Application of nonlinear bayesian filtering for the separation of the MHD effect is thus conceivable, however for standard ECG applications each contributions (e.g. P, QRS and T waves) are temporally separate and thus the Kalman filter has only to consider the evolution of one contribution at a time. Since for the ECG acquisition during MRI, MHD effect waves overlap ECG main waves. The Kalman filter should be able to separate MHD and ECG contribution dynamics, since the dynamics of the contributions are modelled in the equations. However, the model of ECG and MHD is not stationary and the estimation of its evolution will be made difficult if its dynamics are not temporally separated. To overcome this limitation, a new observation equation has been introduced in which a synthetic signal is created by subtracted for the raw ECG observation the prior on the ECG signal (e.g the sum of gaussians of the ECG model given the synthetic phase signal). This new observation gives an approximation of the MHD effect.

The introduction of this new observation relies highly on the priori knowledge of the ECG model. As the ECG signal is nonstationary, the ECG model parameters should be able to evolve during time. The integration of the gaussian parameters inside the state vector has thus been proposed. As no prior knowledge on their evolution can be made, their evolution has been assumed to follow a random walk. The newly introduced observation has thus to be modified to take into account the evolution of the ECG model. The simplest way of incorporating the prior knowledge on the ECG is observing the raw ECG signal, but modifying the observation function, which is then the addition of the MHD contribution and the sum of gaussians whose parameters are in the state vector.

The state space can thus be formulated given the following set of equations:

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The evolution equation being:

$$\begin{aligned}
 \theta_k &= (\theta_{k-1} + \omega\delta) \mod 2\pi \\
 P_k &= -\sum_{i=1}^2 \delta \frac{\alpha_i^{ECG} \omega}{b_i^{ECG^2}} \Delta \theta_{i,k-1}^{ECG} \exp\left(-\frac{\Delta \theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) \\
 &\quad + P_{k-1} + \eta_p \\
 QRS_k &= -\sum_{i=3}^5 \delta \frac{\alpha_i^{ECG} \omega}{b_i^{ECG^2}} \Delta \theta_{i,k-1}^{ECG} \exp\left(-\frac{\Delta \theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) \\
 &\quad + QRS_{k-1} + \eta_{QRS} \\
 T_k &= -\sum_{i=6}^7 \delta \frac{\alpha_i^{ECG} \omega}{b_i^{ECG^2}} \Delta \theta_{i,k-1}^{ECG} \exp\left(-\frac{\Delta \theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) \\
 &\quad + T_{k-1} + \eta_T \\
 MHD_k &= -\sum_i \delta \frac{\alpha_i^{MHD} \omega}{b_i^{MHD^2}} \Delta \theta_{i,k-1}^{MHD} \exp\left(-\frac{\Delta \theta_{i,k-1}^{MHD^2}}{2b_i^{MHD^2}}\right) \\
 &\quad + MHD_{k-1} + \eta_{MHD} \\
 \alpha_{i,k}^{ECG} &= \alpha_{i,k-1}^{ECG} + \varepsilon_{\alpha,i} \\
 b_{i,k}^{ECG} &= b_{i,k-1}^{ECG} + \varepsilon_{b,i} \\
 \xi_{i,k}^{ECG} &= \xi_{i,k-1}^{ECG} + \varepsilon_{\xi,i}
 \end{aligned}
 \tag{2}$$

and the observation equation being

$$\begin{aligned}
 \varphi_k &= \theta_k + v_{1,k} \\
 s_k &= P_k + QRS_k + T_k + MHD_k + v_{2,k} \\
 s_k &= MHD_k + \sum_i \alpha_i^{ECG} \exp\left(-\frac{\Delta \theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) + v_{3,k}
 \end{aligned}
 \tag{3}$$

Each major component of the ECG signal is represented in the state vector, and the estimated ECG signal (z_k) would then be given by the sum of the three components $z_k = P_k + QRS_k + T_k$. The parameters of the gaussians (α_i^{ECG} , b_i^{ECG} and ξ_i^{ECG}) representing the ECG signal are also included in the state vector in order to allow their evolution and thus taken into account their nonstationarity. The gaussian parameters of the MHD contribution are not included in the state vector, even though the signal is nonstationary, but the uncertainty noise η_{MHD} allows us to consider it.

A flow diagram of the method is depicted on figure 2 and flowchart of the bayesian filtering on figure 3.

B. Material

In order to assess the quality of the denoising and the possibility of separating the MHD effect from the ECG signal, it is interesting to apply the method on realistic synthetic signals with additional noise. The computation of SNR of the separated signals will then be possible, since the ECG and MHD signals are known exactly.

The synthetic signals have to be the more realistic, even though not modelling perfectly the real world. It would serve as a first step for proving the applicability of the method on real data, since if the method fails to separate models, then there is no point in trying to apply it on real data. However, it would bias the results to use the same models for both generating the synthetic signal and denoising it.

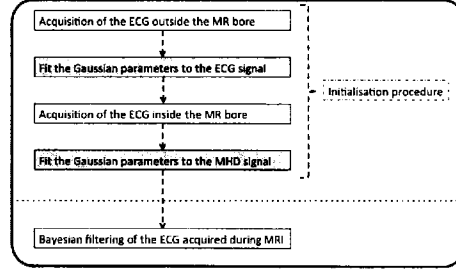


Fig. 2. Flow diagram of the ECG and MHD separation and denoising method.

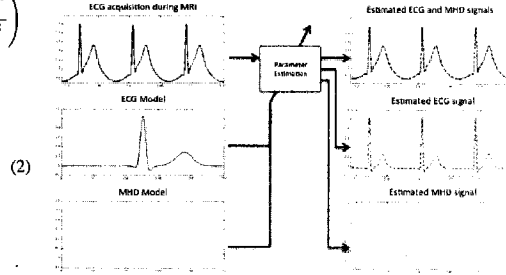


Fig. 3. Flowchart of the bayesian filtering.

An artificial model of MHD effect on the ECG has been recently presented (insert reference to our article) and will be used in this study. The ECG signal has been synthesised with the ECGSim package, which uses a realistic of the heart and torso models for solving the electrophysiological forward problem. The MHD contribution is modelled, by only considered the contribution of the blood flow through the aortic arch, whose 3D model has been computed. The Navier-Stokes equation has been solved for the successive sections with a non conductive rigid wall, and the potential on the torso has been propagated.

ECG have also been acquired in real MRI conditions. Two healthy subjects underwent an MRI examination in a 1.5T GE MR scanner during which ECG signals have been acquired in supine position with three different conditions, firstly the acquisition was performed outside the MR bore i.e. without MHD effect (*the MHD effect can be neglected since the earth magnetic field is relatively low*), secondly two ECG signals were acquired inside the MR bore one with the head-first in and the second feet-first.

III. RESULTS

The results of the denoising and the ECG and MHD separation are depicted on figure 4. Seven gaussians were used for modelling the MHD signal.

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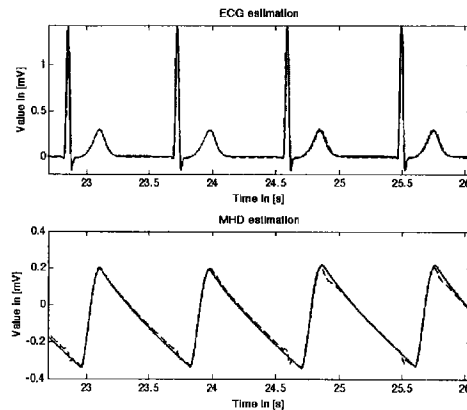


Fig. 4. Separation and denoising of ECG and MHD signals. In blue are depicted the real signal and in dashed red are depicted the estimates. (Top: ECG signal, bottom: MHD signal.)

When focusing on few ECG cycles, the underestimation of the R wave is depictable on figure 4. One can also see that there seems to be some slightly misalignment in the different waves of the ECG signal. The zoom in the MHD estimation allows to show some misestimations occurring during QRS complexes, some little spikes occur during this phase and can be related to the underestimation of the R-wave. Moreover, some estimation error seems also to occur during the T wave, and it seems to be related to the misalignment of the ECG waves estimation.

The signal-to-noise-ratio (SNR) were computed for both the ECG and the MHD estimations and are respectively 19.1dB and 16.2dB. The initial SNR of the ECG signal was 2.6dB and -2.6dB, since the MHD is the noise of the ECG signal and *vice versa*, the SNR improvement is thus respectively 16.5dB and 18.8dB.

The study has also to be conducted with artificial noises (coloured noise and also real noise muscle artefact, electrode movements...)

The same method has been applied on the both subjects by also modelling the MHD contribution with 8 gaussians and results are depicted on figures 5 and 6.

The results on subject 1 are convincing, since the ECG signal extracted from the acquisition is relatively close from the ECG signal acquired outside the MR bore. The evaluation of the quality of denoising is nevertheless not possible since one cannot have an accurate knowledge of the ECG signal while the subject is inside the MR bore.

The estimation of the ECG signal seems less convincing for the subject 2, with a shape of the estimation of the T-wave not completely in accordance with the recording performed outside the MR bore.

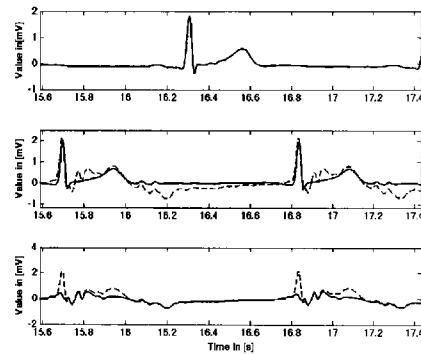


Fig. 5. ECG and MHD separation and denoising on subject 1. (Top: ECG signal without MHD effect. Center: ECG signal estimation in blue and initial ECG signal in red. Bottom: MHD signal estimation in blue and initial ECG signal in red.)

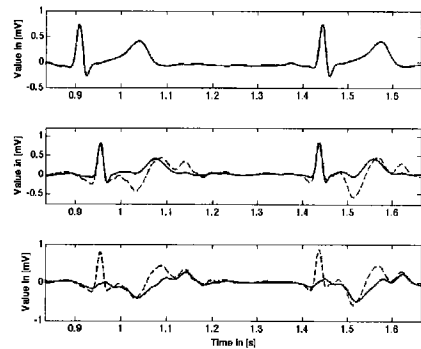


Fig. 6. ECG and MHD separation and denoising on subject 2. (Top: ECG signal without MHD effect. Center: ECG signal estimation in blue and initial ECG signal in red. Bottom: MHD signal estimation in blue and initial ECG signal in red.)

IV. DISCUSSION

V. CONCLUSION

The conclusion goes here.

APPENDIX A

LINEARIZATION OF THE KALMAN FILTER EQUATIONS

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ACKNOWLEDGMENT

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Appendix B

Computer Methods in Biomechanics and Biomedical Engineering
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RESEARCH ARTICLE

Comparison of three artificial models of the MHD effect on the electrocardiogram

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The Electrocardiogram (ECG) is often acquired during Magnetic Resonance Imaging (MRI) for both image acquisition synchronization with heart activity and patient monitoring. Accurate ECG analysis is mandatory for cutting-edge applications, such as MRI guided interventions. Nevertheless, the majority of the clinical analysis of the ECG is made impossible by the occurrence of an artifact called the MagnetoHydroDynamic (MHD) effect. MHD is induced by the flow of electrically charged particles in the blood flowing through the static magnetic field, which creates a potential of the order of magnitude of the ECG.

In this study, a new MHD model is proposed by using MRI based blood flow measurements across the aortic arch. This modeling is extended to several cardiac cycles for allowing the simulation of a realistic ECG acquisition during MRI examination and the quality assessment of MHD suppression techniques.

Comparison of three models and the extracted MHD effect indicates a good agreement between the proposed model and the estimated MHD, but also a better depiction of the complexity of the MHD effect compared to the previously presented models.

Keywords: Electrocardiogram, Modeling, Magnetic Resonance Imaging,
MagnetoHydrodynamic Effect.

1. Introduction

The electrocardiogram (ECG) is an important tool for measuring cardiovascular activity during medical procedures. However, some procedures require an environment which is hostile to ECG acquisition. Magnetic Resonance Imaging (MRI), a noninvasive radiological technique, is a particular case in point. ECG acquisition is required during MRI examinations for two major reasons. Firstly during cardiac MRI applications, acquisitions have to be synchronised with heart activity to reduce motion artefacts in the images (Scott et al. 2009). The ECG is thus used as information on cardiac activity and the QRS complexes are used to initiate MRI acquisitions. This task is known as triggering or gating, and can be performed prospectively or retrospectively. Secondly for safety reason, one wants to ensure that patient physiology is not deteriorating during MRI examination. Physiological parameters are therefore acquired throughout the process (Shellock 2001). Among these physiological parameters, the ECG is one of the most important, since it provides a rapid and standard method to detect conduction and perfusion issues.

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Electrocardiography and MRI make use of electromagnetic fields whether by measuring the fields induced by the heart directly or by exciting the spins of the water particles of the body with the MRI scanner. The ECG is therefore susceptible to interference from the MRI system since the presence of the high static magnetic field distorts the ECG signal, inducing the Hall effect. In the context of fluid flow this is known as the Magnetohydrodynamic (MHD) effect and results from the flow of (charged) blood in the magnetic field as a direct consequence of the Lorentz force $\mathbf{F} = q\mathbf{v} \wedge \mathbf{B}$. The MHD effect thus increases with increased blood flow and when the flow is perpendicular to the magnetic field. Therefore it has been assumed that the effect is mainly induced during blood ejection through the aortic arch (Gupta 2007; Gupta et al. 2008).

Analysis of this effect has been conducted in part due to fears of the hazardous consequences on human physiology, namely the possibility of increased blood pressure, decreased blood flow and interactions between the MHD effect and cardiac pacing. Different studies, ranging from experiments on animals to realistic models with rigid tubes or theoretical analysis with rigid vessels, have concluded that the immersion of human bodies in magnetic field up to 15T is safe. The signal distortion of the ECG has been demonstrated with *in vivo* experiments in various animals (Beischer and Knepton 1964; Togawa et al. 1967; Gaffey et al. 1980; Gaffey and Tenforde 1981; Tenforde et al. 1983; Jehenson et al. 1988; Tenforde 1992, 2005). Noise on the ECG signal has been shown to be correlated with blood flow between heart chambers and also with rapid ejection of blood into pulmonary and aortic vessels. To better understand the phenomenon and predict the physiological effect, theoretical analysis have been conducted, first by approximating the aorta with a rigid vessel with a non conducting wall (Keltner et al. 1990), then by taking into account the conductivity of the vessel wall (Kinouchi et al. 1996; Tenforde 2005) and solving the fluid dynamics with finite element methods. The results of these studies have shown no significant effects on cardiac hemodynamics or function, with a slowing of the blood flow of less than 5% at 10T, an increase in blood pressure of 3% at 8T and the coupling of the magnetic field and blood flow creating current densities at the sinoatrial node region unlikely to produce effects on cardiac pacing under clinical conditions. The major contribution to the MHD effect has been identified as being due to the blood flow in the aortic arch, resulting from geometrical and physiological considerations.

As a consequence, the MHD effect corrupts the ECG immediately after ventricular ejection, which is simultaneous with the ST segment on the ECG. Detection of ischemia is thus practically impossible, since the MHD effect can have a larger amplitude than the R or T-waves. False detection and triggering can therefore be induced leading to motion artefacts on images, especially with the growing use of higher static magnetic field in clinical applications (3 to 7T).

Some specific QRS detectors have been designed to discard MHD effect from QRS complexes (Fischer et al. 1999; Oster et al. 2009). The replacement of the ECG by other cardiac signals, such as heart sounds (Frauenrath et al. 2008) or photoplethysmography has been proposed in order to avoid the distortions due to the MHD effect (Scott et al. 2009). Nevertheless no current methods lead to a signal which can provide an accurate diagnosis of ischemic events. Effective methods to produce a diagnostic quality ECG would be of great clinical benefit. There are three main applications during which this knowledge is useful: 1) MRI guided surgery (McVeigh et al. 2006; Saikus and Lederman 2009; Lederman 2005; George et al. 2011), 2) intracardiac electrophysiology (Susil et al. 2002) and 3) stress testing by MRI (Cheng et al. 2005; Jekic et al. 2008, 2010). However, in order to develop a tool which can provide a useful ECG during MRI, realistic models of the MHD

effect are required. The development of such simulations has thus been a hot topic in recent years. Gupta et al. (2008) suggested the use of the solution for steady flow in rigid vessels and realistic aortic and torso models. Abi-Abdallah et al. (2009) proposed to solve the MHD blood flow problem in presence under physiological pressure gradient. Nijm et al. (2008) suggested the use of realistic inhomogeneous torso model with a simulated blood flow. More recently, some groups proposed the use of finite element techniques in order to simulate the blood flow in arteries and the corresponding potentials on the patient's torso. Kyriakou et al. (2012) proposed to solve the MHD blood flow in a decoupled way, first simulating the blood flow in the primary arteries (aorta, pulmonary arteries) and secondly solving the electromagnetic problem to simulate the MHD effect measured by the ECG electrodes. Lastly, Martin et al. (2012) developed a simulation based on finite element techniques, tackling the blood flow, the heart activity and the diffusion through the torso in a coupled way. In this last simulation, the authors concluded that the ECG acquired inside the MR bore can be approximated by the superposition of the ECG without magnetic field and of the MHD signal, which is proportional to the magnetic field $\mathbf{B}$ and to the flux $\mathbf{q}$ in $\text{cm}^3.\text{s}^{-1}$ as follows;

$$V_i^{ECG}(B_0) \approx V_i^{ECG}(0) + \alpha_i B_0 q, \quad (1)$$

where V_i^{ECG} represents the signal measured on lead i and α_i are given in table 1.

$I(V_1^{ECG})$	$aVR(V_4^{ECG})$	$V_1(V_7^{ECG})$	$V_4(V_{10}^{ECG})$
1.0	-0.67	-0.43	-0.67
$II(V_2^{ECG})$	$aVL(V_5^{ECG})$	$V_2(V_8^{ECG})$	$V_5(V_{11}^{ECG})$
0.35	0.82	-0.14	0.05
$III(V_3^{ECG})$	$aVF(V_6^{ECG})$	$V_3(V_9^{ECG})$	$V_6(V_{12}^{ECG})$
-0.65	-0.15	-0.075	0.12

Table 1. Proportionality coefficients in the equation (1) (in m^{-1}).

We proposed to use MRI based blood flow measurements and artificial blood flow modelled with a sum of Gaussians in order to simulate the MHD effect (Oster et al. 2012).

In this paper we explore and extend a recently described model, indicating deficiencies, and suggesting updates to improve correspondence with real data. ECG recorded during MRI were used to qualitatively validate our model, and the remaining deficiencies are described.

2. Methods

In this work we compare three approaches to generating a realistic model of the MHD effect. First, Realistic geometric models of the torso, heart and aorta are required for accurate simulation of both the ECG and the MHD. These models are presented in subsection 2.1 and will be used for simulating the modelings. The three models compared are:

- (1) The theoretical solution of the Navier-Stokes equation is presented under some assumptions and allows for the simulation of the first MHD modeling in subsection 2.2
- (2) A new modeling based on 4D blood flow measurements across the aortic arch from MRI is proposed in subsection 2.3

(3) A previously presented model in the literature (Martin et al. 2012, 2011).

These three models are compared with an estimation of the MHD effect extracted from real ECG acquisitions during MRI, the method of estimating the MHD effect is presented in subsection 2.4. This section will end with a description of the methodology for the comparison of the models in the subsection 2.5.

2.1 Realistic geometric models

In order to simulate surface ECG measurements, the open source ECGSim package was used to provide a forward model (van Oosterom and Oostendorp 2004). ECGSim contains a realistic 3D model of the heart and the torso, and the electrical activity of the heart's ventricles and provides a solution to the forward problem, resulting in realistic QRST waves on the surface of the body. P waves can be modelled in the recent version of the ECGSim software but were not included in this study, where the focus is on the distortion of ST segment by the MHD effect, and are therefore not relevant.

A model of the aortic arch, developed by Gupta *et al.* (Gupta 2007; Gupta et al. 2008) can describe the three dimensional topology of the vessel as:

$$\begin{aligned} x_A &= R_a(\alpha) \cos(\Psi_a(\alpha)) \cos(\alpha), \\ y_A &= R_a(\alpha) \sin(\Psi_a(\alpha)), \\ z_A &= R_a(\alpha) \cos(\Psi_a(\alpha)) \sin(\alpha), \end{aligned} \quad (2)$$

where α describes a 3D grid such that $\alpha \in [-\frac{3\pi}{24}, -\frac{\pi}{24}, \frac{\pi}{24}, \dots, \frac{27\pi}{24}]$, R_a is the radial function given by

$$\begin{aligned} R_a &= 5.01 \times 10^{-2} \alpha^4 - 3.242 \times 10^{-1} \alpha^3 \\ &+ 5.948 \times 10^{-1} \alpha^2 - 2.504 \times 10^{-1} \alpha + 2.759 \end{aligned} \quad (3)$$

and Ψ_a is the azimuthal angle which is described by

$$\Psi_a = -(\Psi_1 + (\Psi_2 - \Psi_1) \chi(\frac{\alpha}{\Theta})) \cos(2\alpha), \quad (4)$$

with $\Psi_1 = 9.559 \times 10^{-2}$, $\Psi_2 = 1.598 \times 10^{-1}$, $\Theta = 3\pi/4$ and

$$\begin{cases} \chi(s) = 0 & (s < 0) \\ \chi(s) = 3s^2 - 2s^3 & (0 \leq s < 1) \\ \chi(s) = 1 & (s \geq 1) \end{cases} \quad (5)$$

By rotating the model, scaling it and translating it so that the aortic arch starts from the approximate center of the heart, one can make the different models (heart, torso and aorta) match together (see figure 1).

The heart and torso models are oriented such that the backbone is along the z axis. A rotation of a $-\pi/4$ radians around the z axis was then applied, together with a scaling factor of 1.3. Finally the aortic model was translated such that it originates from the 51st node of the heart model. The model of the aorta with

its 16 points in the arch therefore gives 15 sections of one centimeter length. The direction of each section is then computed. As the models are oriented such that the backbone is along the z axis, the magnetic field is also oriented along the z axis.

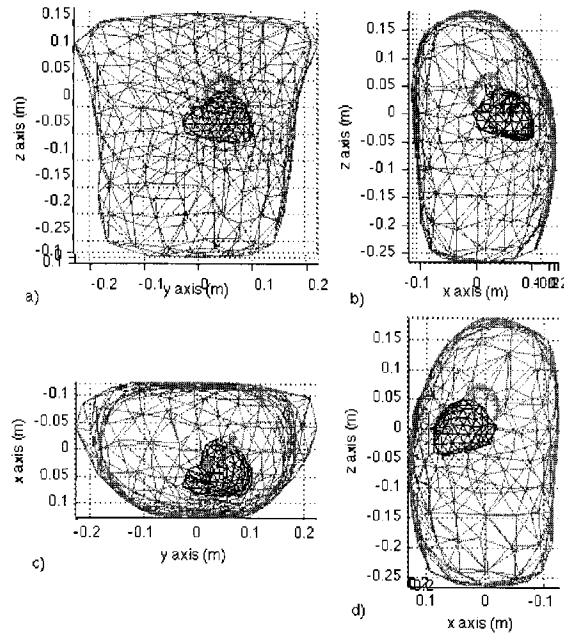


Figure 1. Multiple View of the Geometrical Models. a) Front view, b) lateral view (right side), c) top view, d) lateral view (left side)

The simulation of the MHD effect can be computed by adding the contributions of each of these sections. These contributions can be simulated by computing the pulsed blood flow in this rigid vessel (the aortic arch) under a physiologically realistic gradient pressure (Abi-Abdallah et al. 2009). This pressure profile is the same for each section of the arch except for a delay due to the propagation of the pulse through the aortic arch as in Gupta's paper (Gupta et al. 2008). This delay between two consecutive sections is computed by:

$$\delta t = \frac{L}{V_{PW}}, \quad (6)$$

where V_{PW} is the pulse wave velocity, set to $6.5 m.s^{-1}$ and L is the length of the section (1cm).

Once the body potentials are computed, the resulting ECG signals can be found by using the formulae provided in the ECGSim package. These formulae are determined by the nodes corresponding to the standard electrode placement, which is given in table 2.

Electrode Label	RA	LA	LL	V1	V2	V3	V4	V5	V6
Torso node number	1	2	56	19	26	isocenter(33,34)	41	48	54

Table 2. Correspondance between node number and standard ECG electrode potential locations.

2.2 Theoretical solution using Navier-Stokes

In this section, we will present a theoretical solution from the MHD modeling by extending Abi-Abdallah et al. (2009) works to solve the MHD problem along the aortic arch under simplified assumptions.

2.2.1 General Equations

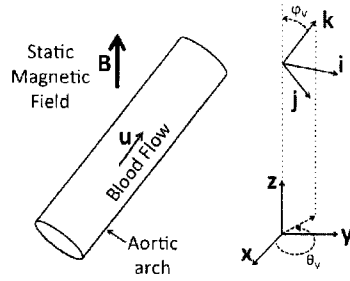


Figure 2. Illustration of the MagnetoHydrodynamic model parametrisation in the aortic arch with a blood flow at velocity $\mathbf{u}$ in direction $\mathbf{k}$. The magnetic field is along the $\mathbf{z}$ direction, and the vessel is along the $\mathbf{k}$ direction. The $(\mathbf{i}, \mathbf{j}, \mathbf{k})$ is defined by: $\mathbf{i} = \sin \theta_V \mathbf{x} - \cos \theta_V \mathbf{y}$, $\mathbf{j} = \cos \varphi_V \cos \theta_V \mathbf{x} + \cos \varphi_V \sin \theta_V \mathbf{y} - \sin \varphi_V \mathbf{z}$ and $\mathbf{k} = \sin \varphi_V \cos \theta_V \mathbf{x} + \sin \varphi_V \sin \theta_V \mathbf{y} + \cos \varphi_V \mathbf{z}$.

Consider a rigid vessel oriented along an arbitrary direction $\mathbf{k}$, such that $\mathbf{k} = \sin \varphi_V \cos \theta_V \mathbf{x} + \sin \varphi_V \sin \theta_V \mathbf{y} + \cos \varphi_V \mathbf{z}$ and immersed in a static magnetic field $\mathbf{B} = B_0 \mathbf{z}$, as shown in figure 2. The Navier-Stokes equation is given by:

$$\rho \left(\frac{\partial \mathbf{u}}{\partial t} + (\mathbf{u} \cdot \nabla) \mathbf{u} \right) = -\nabla p + \eta \nabla^2 \mathbf{u} + \sigma (\mathbf{u} \wedge \mathbf{B}) \wedge \mathbf{B}, \quad (7)$$

where $\mathbf{u}$ is the velocity profile, p is the pressure, η the blood viscosity, σ its conductivity and ρ the blood density. Induced fields are neglected (Abi-Abdallah et al. 2009).

An analytical solution of equation (7) can be calculated (see appendix A) and the flow rate at a cross-section of the arteries can be deduced by integrating over the area of the cross sectional area of the aortic arch as follows

$$q(t) = \int_A \mathbf{u} \cdot \mathbf{k} dA, \quad (8)$$

where A is the cross section of the segment of the aortic arch.

Abi Abdallah *et al.* (Abi Abdallah 2007; Abi-Abdallah et al. 2009) have shown that the resulting dipolar electrical moment is given by

$$\begin{aligned} \mathbf{p} &= \epsilon B_0 \sin \varphi L q(t) \times (\sin(\theta_V) \mathbf{x} - \cos(\theta_V) \mathbf{y}) \\ &= \epsilon B_0 \sin \varphi L q(t) \mathbf{i}, \end{aligned} \quad (9)$$

where ϵ is the dielectric constant of the blood.

The surface body potential, at a point $M = (x_M, y_M, z_M)$ can then be computed as

$$\Phi(M, t) = \frac{B_0 \sin \varphi L \sin(\theta_V) x_M - \cos(\theta_V) y_M}{4\pi} q(t), \quad (10)$$

where $d(M, A) = ((x_M - x_A)^2 + (y_M - y_A)^2 + (z_M - z_A)^2)^{1/2}$ and $A = (x_A, y_A, z_A)$ are the coordinates of the center of the section of the aortic arch.

2.2.2 Pressure profile model

The last component to be computed in order to assess the potential induced by the blood flow in a section of the aortic arch is the pressure gradient, $g(t)$. A widely used model for the aortic pressure is a three-element Windkessel lumped model (Westerhof et al. 1971), which draws an analogy between the pressure profile inside the arteries (in this case) and on electrical circuit. The equivalent diagram is depicted in figure 3.

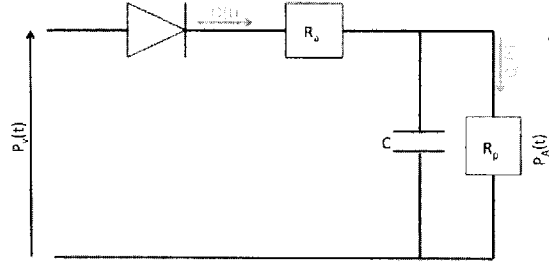


Figure 3. Electrical circuit analogy of the windkessel lumped parametric model, where $P_V(t)$ is the left ventricular pressure, $P_A(t)$ the aortic pressure, $Q(t)$ the output flow rate of the left ventricle, $Q_1(t)$ the input flow rate of the peripheral vessel, R_a the resistance of the aorta, C compliance of the aorta and R_p the resistance of the peripheral arteries.

We then define the ventricular pressure to be

$$P_V(t) = \begin{cases} \frac{P_{max}}{2}(1 - \cos(2\gamma t)) & 0 \leq t \leq t_p \\ 0 & t_p \leq t \leq T \end{cases} \quad (11)$$

with T being the period and t_p being $1/2T$, $\gamma = \pi/t_p$ and P_{max} being the systolic pressure.

Given the Windkessel model, the aortic pressure P_A follows the relationship

$$\frac{dP_A(t)}{dt} + \frac{P_A(t)}{R_p C} = \frac{Q(t)}{C}, \quad (12)$$

where the output flow $Q(t)$ is defined by:

$$Q(t) = \begin{cases} \frac{(P_V(t) - P_A(t))}{R_a} & \text{while } P_V(t) > P_A(t) \\ 0 & \text{else} \end{cases} \quad (13)$$

An analytic solution of the equation (12) has been given by Abi-Abdallah et al. (2009). The flow rate in the aorta can thus be calculated and is shown in figure 4.

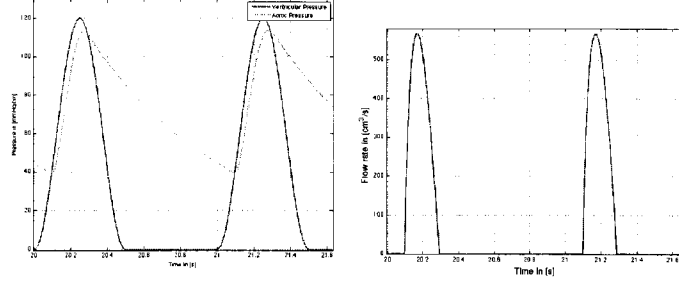


Figure 4. Ventricular and aortic pressures computed by using the three-element Windkessel model (left). Flow rate in the aorta (right).

By assuming that the flow is laminar in the aortic section (with a radius a) the flow is laminar the pressure drop can be approximated by solving the Poiseuille's equation, which is given by:

$$\frac{\Delta P_A(t)}{L} = -\frac{8\eta}{\pi a^4} Q(t) = -\frac{8\eta}{\pi a^4} \frac{\max(0, (P_V(t) - P_A(t)))}{R_A} \quad (14)$$

and thus

$$\frac{\partial p(r, l, t)}{\partial l} = -\frac{8\eta}{\pi a^4} \frac{\max(0, (P_V(t) - P_A(t)))}{R_A}. \quad (15)$$

The gradient pressure profile is defined as $g(t) = -\frac{a^2}{\eta} \frac{\partial p}{\partial l}$ (Abi-Abdallah et al. 2009), and therefore we can conclude

$$g(t) = \frac{8}{\pi a^2} \frac{\max(0, (P_V(t) - P_A(t)))}{R_A}. \quad (16)$$

2.3 MHD modeling based on 4D blood flow measurements from MRI

The theoretical solution of the MHD effect is based on the assumptions that the blood flow is laminar and unidirectional (among other simplifications). These assumptions have been shown to be inaccurate since the blood flow generates vortices and twists, especially in the ascending aorta (Markl et al. 2005; Hope et al. 2007). In order to show these perturbations in the aortic blood flow, Markl *et al.* have used 4D blood flow measured with MRI.

In order to improve the simulation of the MHD effect given in the last section, we make the same type of measurements across the aortic arch. These measurements were then used to determine the dipolar moment the blood flow creates by adapting equation (9). The use of a 4D blood flow measurement makes it possible to observe the nonlinearities in the blood flow. The flow rate will thus have components not

only along the $\mathbf{k}$ direction, but also in the $\mathbf{i}$ and $\mathbf{j}$ directions. These two new components will contribute to the MHD potential on the body torso such that

$$\begin{aligned}\Phi(M, t) &= \Phi_k(M, t) + \Phi_j(M, t) + \Phi_i(M, t) \\ &= \frac{B_0 \sin \varphi L \sin(\theta_V) x_M - \cos(\theta_V) y_M}{4\pi d(M, A)^3} q_k(t) \\ &\quad + \frac{B_0 \cos \varphi L \sin(\theta_V) x_M - \cos(\theta_V) y_M}{4\pi d(M, A)^3} q_j(t) \\ &\quad + \frac{B_0 L - \cos(\theta_V) x_M - \sin(\theta_V) y_M}{4\pi d(M, A)^3} q_i(t),\end{aligned}\quad (17)$$

where $q_i(t)$, $q_j(t)$ and $q_k(t)$ are the blood flow rate in the three different directions measured with MRI.

Measurements were carried on a single subject on a 1.5T General Healthcare (Wawkesha, WI) MRI scanner, after receiving institutional review board ethics approval. Blood flow measurements were realised on four cross sections of the aortic arch with a Phase Contrast Steady State Free Precession (SSFP) Cine sequences (Repetition Time, TR = 10.48ms, Echo time, TE = 5.04ms, flip angle = 20, Field Of View, FOV = 350 × 350mm, 30 cardiac phases, 8 views per segment and Velocity Encoding = 150cm/s).

The imaging slices were placed such that two measurements were realised in the ascending and descending aorta, and two were located in the aortic arch. Their placements are depicted in figure 5. For each plane, the corresponding cross section of the aorta were delineated by hand and the flow rate in the three different directions were computed, by integrating the phase values in the delineated region of interest.

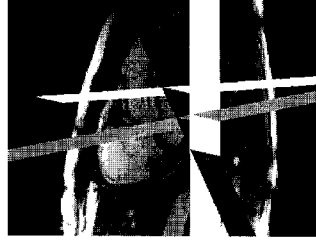


Figure 5. Slices localization and orientation in the aortic arch on anatomical MRI image. (Cyan: ascending aorta, blue: ascending aortic arch, green: descending aortic arch and red: descending aorta).

The aortic model described in section 2.1 was used for computing the contribution of each aortic section for the MHD effect, which contained 15 consecutive segments. Four measurements were taken and so each measurement was used for several sections of the model. The first five aortic contributions were computed by using the flow rate measured in the ascending aorta, the sixth to the eighth sections' contributions by using the cross section in the ascending aortic arch, the ninth to eleventh sections by the measurements in the descending aortic arch and the last sections (i.e. twelfth to fifteenth) were computed with the measurements in the descending aorta.

2.3.1 MHD amplitude correction factor

In our modeling we decided to simplify the forward propagation of the potential on the torso induced by the MHD effect, by computing the torso potential resulting from the radiation of the dipolar electrical moment. Abi Abdallah (2007) has shown that such simplification yields a good approximation of the MHD contribution, but with a slight underestimation of its true value. Recently, the MHD modeling has been recomputed by using realistic geometrical models and numerical methods (Martin et al. 2012, 2011). As explained in the introduction, the MHD model can be expanded with a linear mixing.

Equation (1) can be used in order to find a proportionality factor needed to adjust the amplitude of the simulated MHD effect, $\mathbf{V}^{\text{MHD}}$. This factor, denoted α_{norm} , can be computed by solving first the following linear equation:

$$\mathbf{V}^{\text{MHD}} = \alpha_{\mathbf{q}} \times B_0 \times \mathbf{q}^T, \quad (18)$$

where $\mathbf{q}$ is the norm of the measured flow rate in the second slice. $\alpha_{\mathbf{q}}$ represent the equivalent proportionality coefficients as in equation (1), by assuming the principal contribution of the MHD comes from the flow in the aortic arch. This value can be confirmed by computing the Singular Value Decomposition (SVD) of the MHD effect, $\mathbf{V}^{\text{MHD}}$, and the eigenvector associated with the largest eigenvalue turns out to be approximatively colinear with the vector $\alpha_{\mathbf{q}}$.

Once the $\alpha_{\mathbf{q}}$ have been found, the MHD amplitude correction factor, α_{norm} , can be easily computed with the following relation;

$$\alpha_{\text{norm}} = \frac{\|\alpha\|}{\|\alpha_{\mathbf{q}}\|}. \quad (19)$$

2.3.2 RR interval time series generation

The main purpose of this article is to build a realistic ECG signal simulation during MRI. Applying the above described methodology, we were able to build an artificial signal representing one cardiac cycle of such signal. Nevertheless, we wish to build a continuous signal in order to assess the quality of any denoising method. It is therefore important to build a signal containing several successive cardiac cycles, with their characteristic RR time interval variations. A realistic RR interval time series was simulated with the method proposed by McSharry et al. (2003). This time series has simulated such that its power spectrum consists in a bimodal power spectrum with a sum of two Gaussians distribution. The parameters of these Gaussians determine the frequencies for simulation of the Respiration Sinus Arrhythmia (RSA) and the Mayer waves, but also the ratio of low and high frequencies.

2.3.3 QT interval correction factor

The ECG modeling used in this study only takes into account the ventricular depolarization, that is only the QRS and the T waves are modelled. It has been shown that the diastole and the systole durations do not evolve linearly with the RR interval duration. Several models of QT interval evolution have been presented, among them one of the most famous linking the RR duration with the QT interval through the Bazett formula. However, because we want to be able to study extreme heart rate cases, we have chosen to implement the QT interval relationship with the Fridericia formula (Fridericia 2003), which is given by

$$QTc = QT \times \beta \sqrt[3]{RR}, \quad (20)$$

where β is a constant, which was determined through simulation using ECGsim performed with $RR = 100ms$, such that $\beta = 44.5ms^{2/3}$. The modeling of the ECG signal has thus been linearly stretched between the onset of the Q wave and the offset of the T wave. As the atrial depolarization period has not been modelled in this study, this period was set to 0V.

2.3.4 MHD amplitude fluctuations with the Heart Rate

In this study the modeling of the MHD has been assumed to be induced only by the flow through the aortic arch, which is clearly dependant on the heart rate. The heart can be compared to a pump and the cardiovascular mechanics can easily be modelled. The cardiac output (CO) can be linked to the heart rate (HR) (Mark 2004):

$$CO = \frac{6.9}{0.08 + \frac{3}{HR}} \quad L/min. \quad (21)$$

Since the stroke volume (SV) is the cardiac output divided by the heart rate, one can write

$$SV = \frac{6.9}{0.08HR + 3} \quad L/beat \quad (22)$$

and the stroke volume can be computed from the flow rate by

$$SV = \int q(t)dt \quad (23)$$

By assuming that the MHD effect is only induced by the flow rate, then its integral over the cardiac cycle is proportional to the SV and is thus subject to the same dependency on HR.

The easiest way of taking this dependency into account is to multiply the MHD effect by a SV correction factor and stretch the MHD effect so that it fits the duration of the RR interval (as the stretching procedure does not have an effect on the integral value). The flow measurements have been performed while the subject had a mean HR of 60bpm, thus the SV correction factor, α_{SV} , can be computed from (22) as follows:

$$\alpha_{SV} = \frac{SV(HR)}{SV(60)} = \frac{0.08 \times 60 + 3}{6.9} \frac{6.9}{0.08HR + 3} = \frac{780}{8HR + 300}. \quad (24)$$

2.4 Estimation of MHD using subtraction

The estimation of the MHD model was computed by a simple linear combination of two recordings. The first recording was performed while subject held his breath inside the MR bore in a supine position feet-first (ECG_{ff}). The second recording was performed under the same conditions in a head-first position (ECG_{hf}). Both recordings were 20s long.

The ECG template for each recording was estimated by detecting the QRS complexes and averaging over all cardiac cycles. The two templates were then subtracted and this new template was divided by two. This new template corresponds to a combination of the MHD effect since each recording can be assumed to correspond to ECG plus or minus given the orientation of the patient (Tse et al. 2012).

$$\begin{aligned}
ECG_{hf} &= ECG + MHD \\
ECG_{ff} &= ECG - MHD \\
MHD &= \frac{1}{2}(ECG_{hf} - ECG_{ff})
\end{aligned} \tag{25}$$

2.5 ECG recordings and MHD estimation for comparison of models

As was described in subsection 2.3, a set of blood flow measurements were recorded from a healthy subject. For this subject, ECG recordings have also been realised by using a newly designed and MRI compatible 12-lead ECG monitoring device (Tse et al. 2012). Anatomical imaging of the aortic arch was performed so that one of the parameters of the geometrical model, the angle of the aortic arch, could be set.

The comparison of the MHD model to real recordings was performed first on a single cardiac phase. Three different models, the one described in subsection 2.2 (*theoretical solution*), the one created with the technique described in subsection 2.3 (which is the *proposed model*) and the model computed by equation (1) (*INRIA's model*), were compared with the MHD estimated from the recording (*extracted MHD*).

A quantitative comparison was also conducted by measuring the complexity of the different models. This can be measured by the number of eigenvalues accounting for a certain percentage of the energy. This result will depict the number of components needed for explaining the different models.

3. Results

The depiction of the 12 standard leads with the corresponding MHD model is given in figure 6.

Although the comparison of the different models is mainly qualitative, some conclusions can be made by analysing the figure 6. First, all models have the same appropriate amplitude, showing the amplitude correcting factor for the *proposed model* provides a good approximation and is consistent with the literature. This correcting factor, α_{norm} , is approximately equal to 5, which is within the range described by Abi Abdallah (2007). However, the *theoretical solution* seems to be far too smooth, and this model fails to depict high frequencies present in the *extracted MHD*.

The *proposed model* and *INRIA's model* both seem to be in good agreement with the *extracted MHD*. This is especially true for leads AVL, AVR, AVF, I, II and III. These models seem less in agreement in the precordial leads.

The polarity of the *proposed model* is also in good agreement with the *extracted MHD* effect. One can notice that for most leads, the first wave of the *extracted MHD*, with its peak around 0.15s is well simulated with the *proposed model*. However, we note that the simulated peaks of both the *proposed model* and *INRIA's model* are slightly smoother than the *extracted* ones.

The *extracted MHD* also shows a peak in most leads around 0.6s. These peaks are not present in the three models under consideration, since those are only based on the blood flow in the aortic arch and this peak is not present in the flow measurements across the aortic arch.

The results of the SVD decomposition of the different models (table 3) show that 5 components are needed to account for 99% of the energy of the *extracted model*,

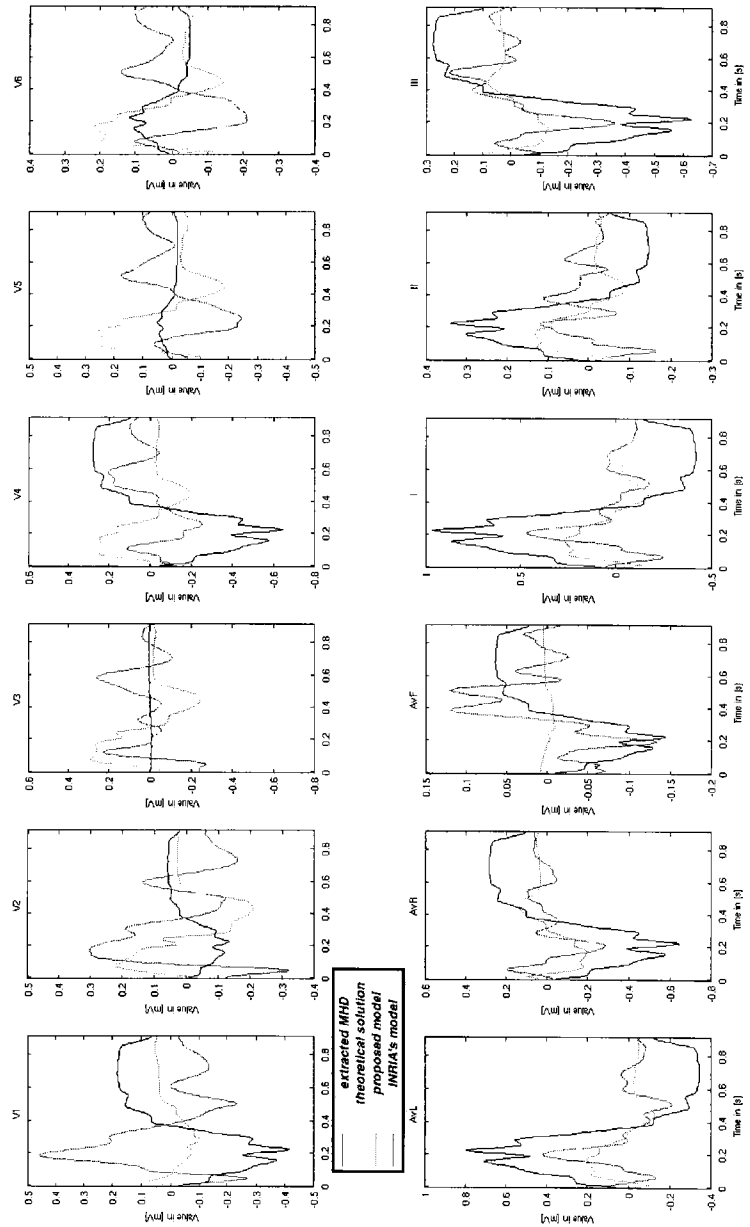


Figure 6. Simulations and estimations of the MHD effects on the 12 standard leads. (blue: extracted MHD, green: theoretical solution, red: proposed model and black: INRIA's model).

number of eigenvalues	<i>theoretical solution</i>	<i>INRIA's model</i>	<i>proposed model</i>	<i>extracted MHD</i>
1	0.9997	1	0.8915	0.7056
2	1	1	0.9992	0.8888
3	1	1	0.9998	0.9438
4	1	1	1	0.9860
5	1	1	1	0.9968
6	1	1	1	0.9990
7	1	1	1	0.9996
8	1	1	1	0.9998
9	1	1	1	1
10	1	1	1	1
11	1	1	1	1
12	1	1	1	1

Table 3. Percentage of energy represented by the eigenvalues.

whereas only one component for both *theoretical solution* and *INRIA's model* and two components for the *proposed model*.

4. Discussion

The smoothness of the *theoretical solution* can be understood by the fact that the rate of flow is a filtered form of the gradient pressure. The filter has a low pass effect, characterized by an impulse response $f(t)$ (See Appendix A). The fact that $f(t)$ corresponds to such a low pass filter comes from the numerous assumptions made when solving the Navier-Stokes equation, especially the laminarity and unidirectionality of the flow. As it has been shown by Markl et al. (2005), the blood flow in aortic arch presents vortices and is twisted, especially in the ascending aorta, which is a result at the manner in which the heart twists as it contracts. These conclusions have been made possible by 4D blood flow measurements in MRI, and therefore the use of these measurements should allow for a better simulation of the MHD effect.

Although the *proposed model* is in good agreement for most leads, morphology are not properly simulated in the precordial leads. This could be due to the way of simulating the propagation through the human torso. Using the ECGSim package, we assumed a linear propagation of the potentials through an homogenous torso. However, if we consider a more complicated propagation of this potentials, such as in Kyriakou et al. (2012), the potentials in the electrodes close the heart are very sensitive to slight positioning errors. Therefore, by using a standard average torso model which does not correspond to the patient's anatomy, dramatic changes in the MHD effect morphology will result.

The first peak of the *extracted MHD* is well simulated in most leads with the *proposed model*, nevertheless the *extracted MHD* contains higher frequencies and the *proposed model* seems to be a smoothed version of the *extracted MHD*. One explanation of such a phenomenon could come from the MRI based method for measuring the blood flow in the aortic arch. One limitation of this method is the relatively low temporal resolution achievable for the measurement due to the heart motion and the intrinsic properties of MRI acquisition. Moreover the blood flow is measured over several cardiac cycles (approximately twenty) and the blood flow pattern obtained is thus averaged over these cycles, which could explain the smoothing. The same conclusion can be made with the *INRIA's model* since it is also based on the blood flow measurement in the ascending aorta.

A second important peak is also present in the *extracted MHD* around 0.6s, this peak is not simulated with the proposed method. This can be explained by the fact that the proposed method only considers the contribution from the blood flow in the aortic arch. Kyriakou et al. (2012) have analysed the contributions of other arteries, such as the pulmonary arteries. These contributions have been shown not to

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contribute greatly, and they cannot explain the presence of this second peak, since the blood flow in these arteries occur simultaneously with the flow in the aortic arch. Nevertheless, the MHD is the sum of the contributions from all the arteries in the human body and the 0.6s peak could represent a cumulative contribution from major arteries such as the carotid, femoral, subclavian and perhaps even brachial arteries. Adding all these contributions could allow for a better simulation of the high frequencies present in the extracted MHD effect. One contribution that has not been considered in known simulations is the blood filling of the ventricles even if this flow is important and located near the electrodes and can thus have an important influence over the MHD effect. It would be interesting to simulate this effect by measuring the blood flow inside the ventricles, by locating the measurement plane just after the valves. Unfortunately these measurements were not available from our recordings.

The introduction of the *proposed model* has been interesting for several reasons. First it increases our understanding of the phenomenon, and in particular shows that the main contribution of this MHD effect comes effectively from the aortic arch. However other contributions should be considered for complete simulation of the MHD phenomenon. The *proposed method* reflects more adequately the reality than the simplified equation proposed by Martin et al. (2012). Applying SVD to the *extracted MHD* clearly shows that this effect is more complex than a simple eigenvector as suggested by Martin et al. (2012).

5. Conclusion

In conclusion, this study allows for the development of a realistic MHD model. The *proposed model* focuses on the aortic arch contribution, which is the most important in the situation where the magnetic field orientation is along the body axis, as in most clinical MRI. The MHD was modelled with blood flow measurements performed along the aortic arch, and the *proposed model* was shown to be in good agreement with the extracted MHD. Such agreement shows that if we are able to simulate the MHD effect from blood flow measurements in the aortic arch, then conversely we should be able to extract important clinical information like the Cardiac Output from the extracted MHD, as suggested by Tse et al. (2012).

Improvements could be added to this modeling by considering blood flow circulation in more arteries as was suggested by Kyriakou et al. (2012). It seems however that given the localization in time of an important peak in the MHD, the blood circulation in the heart ventricles should be playing an important role in the creation of the MHD effect.

Lastly, although we have identified several deficiencies in current MHD modeling techniques, the new model presented here captures much of the MHD effect superimposing the ECG during MRI and should provide a useful tool for preliminary assessment of ECG denoising and MHD suppression techniques (Oster et al. 2012).

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Appendix A. Analytical solution of the Navier Stokes equation

Let (r, θ, l) be the cylindrical coordinates in the $(O, \mathbf{i}, \mathbf{j}, \mathbf{k})$ reference frame. Let us also assume that the flow is laminar, axisymmetric and unidirectionnel. The fluid velocity can then be written as $\mathbf{u} = u_l(r, l, t)\mathbf{k}$. As the blood can be considered as an incompressible fluid, $\nabla \cdot \mathbf{u} = 0$ and as the flow is considered unidirectional $u_\theta = u_r = 0$. One can then conclude that since $\nabla \cdot \mathbf{u} = \frac{1}{r} \frac{\partial}{\partial r}(ru_r) + \frac{1}{r} \frac{\partial u_\theta}{\partial \theta} + \frac{\partial u_l}{\partial l} = 0$, then $\frac{\partial u_l}{\partial l} = 0$, and thus $\mathbf{u} = u_l(r, t)\mathbf{k}$. The vector Laplacian of the fluid velocity is also given by $\nabla^2 \mathbf{u} = (\frac{\partial^2 u_l}{\partial r^2} + \frac{1}{r} \frac{\partial u_l}{\partial r})\mathbf{k}$.

Taking into account that:

$$\begin{aligned} \mathbf{u} \wedge \mathbf{B} &= u_l(r, t)\mathbf{k} \wedge B_0 \mathbf{z} \\ &= u_l(r, t)B_0(\sin \varphi_V \cos \theta_V \mathbf{x} + \sin \varphi_V \sin \theta_V \mathbf{y} + \cos \varphi_V \mathbf{z}) \wedge \mathbf{z} \\ &= u_l(r, t)B_0(\sin \varphi \sin \theta_V \mathbf{x} - \sin \varphi \cos \theta_V \mathbf{y}), \end{aligned} \quad (\text{A1})$$

one have

$$\begin{aligned} (\mathbf{u} \wedge \mathbf{B}) \wedge \mathbf{B} &= -u_l(r, t)B_0^2(\sin \varphi \cos \theta_V \mathbf{x} + \sin \varphi \sin \theta_V \mathbf{y}) \\ &= -u_l(r, t)B_0^2 \sin \varphi (\cos \theta_V \mathbf{x} + \sin \theta_V \mathbf{y}) \\ &= -u_l(r, t)B_0^2 \sin \varphi (\sin \varphi \mathbf{k} + \cos \varphi \mathbf{j}). \end{aligned} \quad (\text{A2})$$

By projection onto the vector $\mathbf{k}$, equation (7) can then be rewritten as:

$$\rho \frac{\partial u_l}{\partial t} = -\frac{\partial p}{\partial l} + \eta \frac{\partial^2 u_l}{\partial r^2} + \eta \frac{1}{r} \frac{\partial u_l}{\partial r} - \sigma B_0^2 \sin^2 \varphi u_l. \quad (\text{A3})$$

Multiplying equation (A3) by $\frac{a^2}{\eta}$ and defining $y = \frac{r}{a}$, where a is the radius of the vessel, we have

$$\begin{aligned} \frac{a^2}{\nu} \frac{\partial u_l(y, t)}{\partial t} &= -\frac{a^2}{\eta} \frac{\partial p}{\partial l} + \frac{\partial^2 u_l(y, t)}{\partial y^2} + \frac{1}{y} \frac{\partial u_l(y, t)}{\partial y} \\ &\quad - \sigma \frac{a^2}{\eta} B_0^2 \sin^2 \varphi u_l(y, t). \end{aligned} \quad (\text{A4})$$

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Defining $g(t) = -\frac{a^2}{\eta} \frac{\partial p}{\partial t}$ and $\sigma \frac{a^2}{\eta} B_0^2 \sin^2 \varphi = H_a^2$ (the squared Hartmann number), equation (A5) becomes

$$\frac{a^2}{\nu} \frac{\partial u_l(y, t)}{\partial t} = g(t) + \frac{\partial^2 u_l(y, t)}{\partial y^2} + \frac{1}{y} \frac{\partial u_l(y, t)}{\partial y} - H_a^2 u_l(y, t). \quad (\text{A5})$$

To solve this equation, we can employ a method based on Fourier and Hankel transforms. Applying the following Fourier transforms:

$$u_l(y, t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} U_l^y(\omega) e^{j\omega t} d\omega, \quad (\text{A6})$$

$$g(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} G(\omega) e^{j\omega t} d\omega, \quad (\text{A7})$$

equation (A5) becomes:

$$\frac{a^2}{\nu} j\omega U_l^y(\omega) = G(\omega) + \nabla^2 U_l^y(\omega) - H_a^2 U_l^y(\omega), \quad (\text{A8})$$

where,

$$\nabla^2 U_l^y(\omega) = \frac{\partial^2 U_l^y(\omega)}{\partial y^2} + \frac{1}{y} \frac{\partial U_l^y(\omega)}{\partial y}. \quad (\text{A9})$$

The Hankel transform is defined as:

$$H\{f(r)\} = F^*(n) = \int_0^1 r f(r) J_0(r\lambda_n) dr, \quad (\text{A10})$$

and

$$f(r) = 2 \sum_{n=1}^{\infty} \frac{J_0(\lambda_n r)}{J_1(\lambda_n)^2} F^*(n), \quad (\text{A11})$$

and where J_n is the n^{th} order Bessel functions, λ_n are the roots of the J_0 . The Hankel transform has the following properties:

$$H\{\nabla^2 f(r)\} = -\lambda_n^2 F^*(n) \text{ (if } f(1) = 0), \quad (\text{A12})$$

$$H\{c\} = \frac{c}{\lambda_n} J_1(\lambda_n), \quad (\text{A13})$$

with c being a constant.

Applying Hankel transform to equation (A8) yields

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$$\frac{a^2}{\nu} j\omega U_{l\omega}^*(n) = \frac{G(\omega)}{\lambda_n} J_1(\lambda_n) - \lambda_n^2 U_{l\omega}^*(n) - H_a^2 U_{l\omega}^*(n). \quad (\text{A14})$$

The value of $U_{l\omega}^*(n)$ can thus be computed:

$$U_{l\omega}^*(n) = \frac{J_1(\lambda_n)}{\lambda_n \left(\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2 \right)} G(\omega). \quad (\text{A15})$$

Applying the inverse Hankel transform then gives

$$U_l^y(\omega) = 2 \sum_{n=1}^{\infty} \frac{J_0(\lambda_n r)}{J_1(\lambda_n)^2} \frac{J_1(\lambda_n)}{\lambda_n \left(\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2 \right)} G(\omega). \quad (\text{A16})$$

Finally, we obtain the velocity profile by applying the inverse Fourier transform to $U_l^y(\omega)$ such that

$$u_l(y, t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} 2 \sum_{n=1}^{\infty} \frac{J_0(\lambda_n y)}{J_1(\lambda_n)^2} \frac{G(\omega)}{\lambda_n \left(\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2 \right)} e^{j\omega t} d\omega, \quad (\text{A17})$$

and

$$u_l(y, t) = \frac{1}{\pi} \sum_{n=1}^{\infty} \frac{J_0(\lambda_n y)}{J_1(\lambda_n) \lambda_n} \int_{-\infty}^{\infty} \frac{G(\omega)}{\left(\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2 \right)} e^{j\omega t} d\omega. \quad (\text{A18})$$

The integral

$$\int_{-\infty}^{\infty} \frac{G(\omega)}{\left(\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2 \right)} e^{j\omega t} d\omega \quad (\text{A19})$$

is equivalent to the inverse Fourier transform of

$$FT^{-1} \left\{ G(\omega) \frac{1}{\left(\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2 \right)} \right\}, \quad (\text{A20})$$

which in the time domain can be written

$$g(t) * FT^{-1} \left\{ \frac{1}{\left(\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2 \right)} \right\}, \quad (\text{A21})$$

where $*$ denotes the convolution operator.

To solve the inverse transform in equation (A21), we apply the following Fourier transform pair:

$$h(t)e^{-\alpha t} \rightarrow \frac{1}{\alpha + j\omega}, \quad (\text{A22})$$

where h is the Heaviside step function, the integral of the Dirac delta function, $h(t) = \int_{-\infty}^t \delta(x)dx$.

We can therefore express the inverse Fourier Transform of equation (A21) as:

$$\begin{aligned} FT^{-1} \left\{ \frac{1}{\frac{a^2}{\nu} j\omega + \lambda_n^2 + H_a^2} \right\} &= FT^{-1} \left\{ \frac{\nu}{a^2} \cdot \frac{1}{j\omega + \frac{\nu}{a^2} (\lambda_n^2 + H_a^2)} \right\} \\ &= \frac{\nu}{a^2} e^{-\frac{\nu}{a^2} (\lambda_n^2 + H_a^2)t} h(t). \end{aligned} \quad (\text{A23})$$

Finally, we obtain the velocity profile as

$$u_l(y, t) = g(t) * \frac{1}{\pi} \sum_{n=1}^{\infty} \frac{J_0(\lambda_n y)}{J_1(\lambda_n) \lambda_n} \frac{\nu}{a^2} e^{-\frac{\nu}{a^2} (\lambda_n^2 + H_a^2)t} h(t). \quad (\text{A24})$$

Given this velocity profile, the rate of flow, q , corresponds to:

$$q(t) = 2\pi a^2 \int_0^1 u_l(y, t) y dy, \quad (\text{A25})$$

which is

$$q(t) = g * 2 \sum_{n=1}^{\infty} \left(\frac{1}{J_1(\lambda_n) \lambda_n} \nu e^{-\frac{\nu}{a^2} (\lambda_n^2 + H_a^2)t} h(t) \times \int_0^1 J_0(\lambda_n y) y dy \right). \quad (\text{A26})$$

Taking into account that $\int x^n J_{n-1}(x) dx = x^n J_n(x)$, the flow rate becomes

$$q(t) = (g * f)(t), \quad (\text{A27})$$

where $g(t) = -\frac{a^2}{\eta} \frac{\partial p}{\partial t}$ m/s, and $f(t) = 2 \sum_{n=1}^{\infty} \frac{1}{\lambda_n^2} \nu e^{-\frac{\nu}{a^2} (\lambda_n^2 + H_a^2)t} h(t)$.

Finally, the electrical potential induced on the vessel walls is given by

$$V(t) = \frac{2B_0 \sin \varphi}{\pi a} q(t). \quad (\text{A28})$$

Appendix C

1 Purpose

Electrocardiogram (ECG) acquisitions are performed widely during clinical MRI. The MRI environment highly distorts ECG acquisitions and complicates its analysis. The MagnetoHydroDynamic (MHD) effect, induced by the static magnetic field, makes cardiac MRI applications challenging especially on high field systems or during interventions where ST segment analysis could be of great help. The MHD effect has been shown to be mainly induced by the blood flow through the aortic arch [1]. In this study, an accurate ECG and MHD modeling is presented. This modeling is based on the solution of MHD equations for the aortic arch [2], and on the Uniform Double Layer model for ECG simulation [3].

2 Methods and Materials

The ECGSIM package was used for ECG simulation, and for the torso and heart models [3]. The MHD equations were solved to estimate the equivalent dipole resulting from the static magnetic in a section of the aortic arch under a realistic pulse pressure profile [2], and the resulting potential on the torso was computed, by using a realistic equation for the aortic arch geometry [1].

The aortic arch was divided into fifteen sections of rigid cylindrical sections of 1 cm length. The aortic pulse pressure profile, required to solve Navier-Stokes equation, was modelled with a lumped three-element windkessel model. The contribution of each section was computed, projected onto the torso and combined.

These simulations were compared with ECG acquisitions performed on a 1.5T and a 3T MR system. These acquisitions were performed in supine position both head-first and feet-first, so the MHD effect could be estimated by linear transform [4].

3 Results

Figure 1: 3D geometrical models of heart, torso and aortic arch.

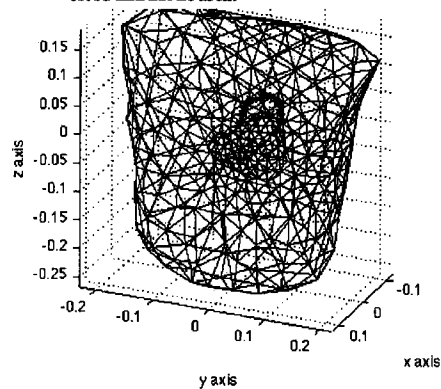
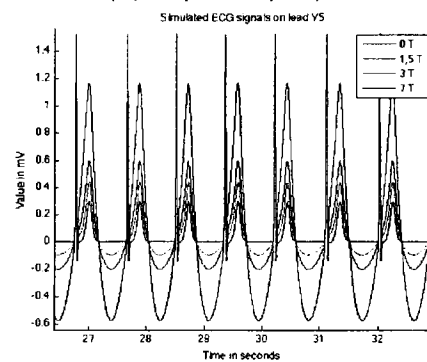


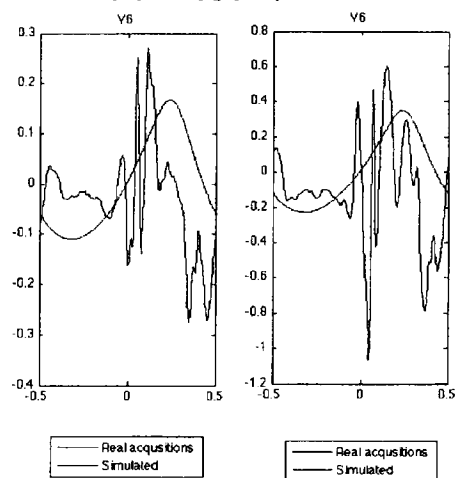
Figure 1 illustrates the 3D models used for the simulation of ECG and MHD model. The resulting ECG simulation while patient is immersed in different magnetic field strength is presented in figure 2.

Figure 2: ECG and MHD simulation on lead V5
in different magnetic field strengths
(subject in supine head-first position)



Comparison of simulated MHD effects and estimated effects at 1.5 T and 3 T are given in figure 3.

Figure 3: Comparison of estimated (blue) and simulated (red) MHD effects
on lead V6 in 1.5 T (left) and 3 T (right) MR systems.



4 Conclusion

A realistic, but highly simplified model of ECG acquisition with MHD contamination in different fields has been described. Although the proposed model underestimates the higher frequency contributions of the arteries in the human body other than the aorta, the simulation is in general agreement with real data. The simulation of this effect will allow to work on the MHD effect suppression techniques that are required for enhancing the accuracy of high field cardiac MRI and increasing patient safety during MR guided interventions.

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5 Mesh

Biomedical engineering [J01.293.143]

6 Keywords

Electrocardiogram, modelling, MagnetoHydroDynamic

Appendix D

Tracking arrhythmias in the ECG using a switching Kalman filter

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Abstract

Automatic processing and accurate diagnosis of pathological Electrocardiogram (ECG) signals remain a challenge. A model-based ECG filtering approach has been recently proposed and successfully applied to healthy subjects, opening a way for elegant and accurate online analysis of physiological signals.

The same approach has been introduced for detecting arrhythmias and more particularly Premature Ventricular Contraction (PVC). In this paper, an extension of this approach is proposed for which normal but also abnormal beats, such as PVC, are modelled. The technique is allowed to switch to the most likely mode and filters the signal by using the most appropriate prior knowledge.

The technique has been applied on a simulated realistic ECG recording with real noise data. Results show a promising 100% accuracy for arrhythmia detection. Moreover the signal quality enhancement allows automatic QT measurement to be improved such that its error (8.95ms) stays within range of the error made by human annotators.

1. Introduction

Electrocardiogram (ECG) analysis is routinely used in clinical practice for the diagnosis of cardiovascular diseases. It is the state-of-the-art for the detection of arrhythmias, and more specifically Premature Ventricular Contraction (PVC). PVC is a contraction of the heart, which has been initiated in the ventricle after spontaneous repolarization of ventricle cells (ectopic focus) or re-entrant signalling. PVC generates thus a different ECG pattern than normal heart beats originated from the sinoatrial node. Occurrence of PVCs is an indicator of cardiovascular risks, such as sudden cardiac death or myocardial infarction [1].

Development of accurate automated ECG analysis techniques has been a challenge for the last decades and several methods have been suggested for the automatic detection and classification of arrhythmias [2].

Recently, a model-based ECG denoising has been proposed by applying Extended Kalman Filter (EKF) [3].

This technique has been successfully applied to signal denoising, but also to the detection of premature ventricular detection [2]. In this paper, the latter work will be extended, in order to apply the model-based filtering on the ECG, by taking into consideration a model for the PVC beats and also allowing an X factor mode, i.e. an unknown beat (whether artifacts or unknown pathological beat). The filter will be able to switch modes automatically to better fit the observations and thus allow accurate ECG analysis, such as QT measurement, for pathological rhythms.

2. Theory

2.1. Model-based ECG filter

ECG signal can be modelled as a pseudo periodic signal, each cycle being a sum of Gaussians [4]. It has been shown that the use of seven Gaussians, the first two representing the P wave, the next three the QRS complex and the last two the T wave, allows accurate representation of the ECG signal [2]:

$$\begin{cases} \theta_k = (\theta_{k-1} + \omega\delta) \bmod 2\pi \\ z_k = - \sum_i \delta \frac{\omega \Delta \theta_{i,k-1}}{b_i^2} G(\alpha_i, \Delta \theta_{i,k-1}, b_i) + z_{k-1} + \eta \end{cases} \quad (1)$$

where θ_k is the angular position in the cylindrical coordinates, $\omega = 2\pi/RR$ the angular speed, δ the sampling period. z_k represents the ECG value in mV at time k and α_i, b_i, ξ_i are the amplitude, width and angular position of the i^{th} Gaussian respectively, with $\Delta \theta_{i,k-1} = (\theta_{k-1} - \xi_i) \bmod 2\pi$ and with $G(a, b, c) = a \exp(-\frac{b^2}{2c^2})$ a Gaussian wave. Let call a mode the given dynamical model explaining the time-dependent evolution of a cardiac cycle.

The denoising of the ECG signal is then performed by non-linear Bayesian filtering, the Gaussian parameters of the underlying model being initialised beforehand. State-space formalism is thus required, which can be formulated using the following set of equations [2]:

(i) evolution equations,

$$\begin{cases} \theta_k = (\theta_{k-1} + \omega\delta) \bmod 2\pi \\ P_k = -\sum_{i=1}^2 \delta \frac{\omega \Delta \theta_{i,k-1}}{b_{i,k-1}^2} G(\alpha_{i,k-1}, \Delta \theta_{i,k-1}, b_{i,k-1}) \\ \quad + P_{k-1} + \eta_P \\ C_k = -\sum_{i=3}^5 \delta \frac{\omega \Delta \theta_{i,k-1}}{b_{i,k-1}^2} G(\alpha_{i,k-1}, \Delta \theta_{i,k-1}, b_{i,k-1}), \\ \quad + C_{k-1} + \eta_{QRS} \\ T_k = -\sum_{i=6}^7 \delta \frac{\omega \Delta \theta_{i,k-1}}{b_{i,k-1}^2} G(\alpha_{i,k-1}, \Delta \theta_{i,k-1}, b_{i,k-1}) \\ \quad + T_{k-1} + \eta_T \end{cases} \quad (2)$$

(ii) observation equations,

$$\begin{cases} \varphi_k = \theta_k + v_{1,k} \\ s_k = P_k + C_k + T_k + v_{2,k} \end{cases}, \quad (3)$$

where P , C and T represent the P wave, the QRS complex and the T wave respectively. $(\alpha_{i,k}, \Delta \theta_{i,k}, b_{i,k}, \xi_{i,k})$ are the Gaussian parameters for the ECG signal (P, QRS and T waves). The observed signal, s_k is the ECG signal and φ_k is an artificial phase signal assigned linearly from 0 to 2π between two consecutive R waves and then rescaled between $-\pi$ and π . Each major component of the ECG signal is represented in the state vector, and the denoised ECG signal (z_k) is then given by the sum of the three components $z_k = P_k + C_k + T_k$.

2.2. Switching Kalman Filter

The approach of model-based filtering has been shown to be powerful for healthy subjects and a measure of accordance between the observations and the model has been successfully introduced for the detection of PVC. In highly non-stationary situations, such as ECG signals with pathological rhythms (bi- or tri-geminy), this approach is less suited since the model which is supposed to provide a strong *prior* on the signal does not correspond to the observation.

This problem has been encountered previously in biomedical applications and physiological condition monitoring [5]. Switching Kalman Filters has been proposed to solve this problem, where a random signal can be approximated by different state-space formalisms depending on its mode [6]. In such approach, for each new sample the Kalman filter is computed for each mode and the likelihood is then used to choose which mode is best suited to the observation.

Let call $H^{(i)}$ the observation matrix of the i^{th} mode, such that $y = H^{(i)} \times x^{(i)} + v^{(i)}$ and let denote $R^{(i)} =$

$cov(v^{(i)})$, the covariance of the observation noise. The innovation at time k , is denoted $\tilde{y}_k^{(i)} = y_k^{(i)} - H^{(i)} \times \hat{x}_k^{(i)}$ and $R_e^{(i)}$ its covariance, which can be computed with:

$$R_e^{(i)} = R^{(i)} + H^{(i)} P_{(k-1,k)}^{(i)} H^{(i)T}, \quad (4)$$

with $P_{(k-1,k)}^{(i)}$ being the *prior* state covariance matrix, which is computed step by step during the Kalman filter procedure.

The residual likelihood for this mode, $L(i)$, can then be computed by:

$$L(i) = \frac{1}{\alpha} \frac{1}{\sqrt{2\pi \det(R_e^{(i)})}} \exp\left(-\frac{1}{2} \tilde{y}_k^{(i)T} R_e^{(i)-1} \tilde{y}_k^{(i)}\right), \quad (5)$$

with α being a normalization factor, so that $\sum_i L(i) = 1$.

2.3. X-Factor, naive modeling

Switching Kalman Filters framework is well-designed for situations where the model for each mode is known or can be initialized. Nevertheless for some situations such as spontaneous PVC occurrence in healthy subject, the model cannot be initialized since their occurrence rate is low.

Quinn *et al.* have dealt with such situation by introducing a new mode, called the X-factor [5]. In this study, we adapt a similar approach by considering the ECG filtering as a tracking problem, and the ECG value having an almost constant "speed", which will be thereafter referred as naive modeling. The state-space formalism can be written as follows:

(i) evolution equations

$$\begin{cases} x_k = x_{k-1} + \frac{dx_{k-1}}{f_s} + v_{1,k} \\ dx_k = dx_{k-1} + v_{2,k} \end{cases}, \quad (6)$$

f_s being the sampling frequency, x_k , dx_k being the position and speed of the target and v_k being the state noise.

(ii) observation equations

$$s_k = x_k + v_{1,k}, \quad (7)$$

s_k being the observed signal (ECG) and $v_{1,k}$ the observation noise.

3. Material & Method

3.1. Data

The proposed method was applied on a five and half minutes long synthetic ECG signal with a 1000Hz sampling frequency.

The ECG was modelled with the dynamical VCG model, that represents each of the three axis of the VCG

by a sum of Gaussians and then applied a Dower transform [7]. Three modes were used, (i) a normal heartbeat, (ii) a PVC originating from one ectopic focus (*PVC1*) and (iii) a PVC from another ectopic beat (and then having a different shape) (*PVC2*). The State Transition Matrix ($STM(i, j) = Pr(Mode(k) = i | Mode(k-1) = j)$) has been set as:

$$STM = \begin{bmatrix} 2/3 - 0.1 & 0.99 & 1 \\ 1/3 & 0.01 & 0 \\ 0.1 & 0 & 0 \end{bmatrix}$$

Finally, to generate realistic recordings, real noise was added from the Noise Stress Test Database [8,9]. Muscle artefact and baseline wander noise, recorded from limbs without ECG contamination, were superimposed on the artificial ECG at realistic levels. The two leads of the noise data recordings were added onto VCG leads X and Y. The third lead was simply generated as the first principal component of the two others [10]. The level of noise added corresponded to a 3dB Signal to Noise Ratio (SNR).

3.2. Method

Preprocessing

A 2nd order Butterworth high-pass filter, with a 0.5Hz cut-off frequency, is first applied to the ECG signal in order to attenuate the baseline wander.

Gaussian Parameters Initialization

The first 30s of the recording were used for the initialization of the Gaussian parameters. Each new cardiac cycle detected was compared with known cycle of each mode, and if the normalised cross-correlation was higher than a set threshold (0.9), this cycle was added to the mode. If the new cycle was not classified as an existing mode, a new mode was created and was represented by this given cardiac cycle.

If a mode was represented by more than five cycles, then a nonlinear fitting of seven Gaussian parameters was performed. Let denote n the number of modes for which the Gaussian parameters have been initialized.

Application of the Switching Extended Kalman Filter

The nonlinear Bayesian filtering was then applied on the last five minutes of recording. Extended Kalman Filter (EKF) was thus performed on the three VCG leads in parallel for the $n + 1$ different modes, i.e. the n Gaussian based models previously initialized and the naive modeling introduced in subsection 2.3.

The artificial phase signal φ gives information on the length of a cardiac cycle. The mode likelihood $M(i)$ was computed for each mode as the mean of the residual likelihood ($L(i)$ in equation (5)) over the cardiac cycle. The mode minimizing this likelihood for a given cardiac cycle, was selected and the signal estimated for this mode is considered as the denoised ECG during the current heart beat.

3.3. Quality assessment

The method was first assessed regarding the accuracy for the mode estimation.

Moreover the quality of denoising was assessed. While SNR improvement computation could have easily been performed. We were more interested in the diagnostic quality of the signal and especially the QT measurement. Ecgpuwave algorithm was therefore applied for ECG segmentation [9, 11]. The QT intervals of normal beats were then measured before and after filtering, and compared with the measurements performed on the clean ECG.

4. Results

The initialization procedure provided two modes for which the Gaussian parameters have been estimated, corresponding to the normal and the *PVC1* beats. Consequently the *PVC2* beats were represented by the naive modeling.

The method processed the simulated ECG signal with an impressive 100% accuracy. The quality of denoising and mode estimation is depicted on figure 1.

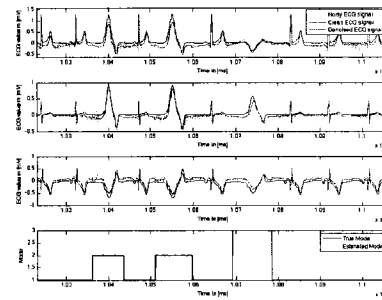


Figure 1. ECG Signal denoising (three figures on top represent respectively VCG leads X, Y and Z) and Mode Estimation (bottom).

The measurements of the QT intervals are depicted on figure 2.

The mean absolute difference (MAD) between the measurements on clean and noisy ECG before denoising is 27ms, which is slightly higher than the manual estimation errors[12]. The MAD between the measurements on the clean and denoised ECG is 8.95ms, which is below the manual annotations error.

However, the automatic segmentation algorithm used was unable to detect the T wave offset for several cardiac cycles on the denoised ECG. This phenomenon occurred mostly on normal beats preceeding a *PVC1* beat.

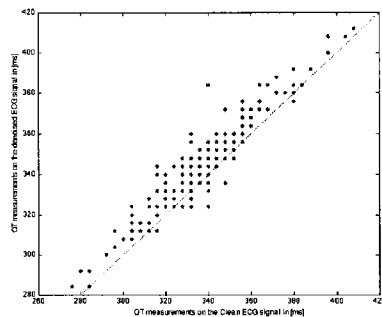


Figure 2. Comparison of the QT measured on a clean ECG signal (x axis) and on the denoised ECG signal (y axis).

5. Discussion

The accuracy of the classification result shows a promising way of detecting abnormal beats, both when the abnormal beat has been modelled, as for *PVC1*, and in the case where no *prior* knowledge on the abnormal beat was available as for *PVC2*.

In the same way, the QT measurements enlighten that the denoised ECG signal quality is suitable for accurate analysis and diagnosis.

However, the present results were obtained on only one simulated signal. These promising results need thus to be confirmed on real data and on a larger database before further conclusions can be drawn.

There is still room for improvement for this technique. The inability of the automatic segmentation to detect T wave's offset for some normal beats preceeding a change in mode is a clear limitation. This phenomenon could be induced by the handling of ECG signal estimation at the moment of a change in mode. The state variables of the correct mode could be used as an initialization value for all modes at each new cardiac cycle. This is currently not performed, since the Bayesian filtering is applied independently for each mode in parallel.

When considering applications with longer recording, as Holter recordings, the method should also be able to take into consideration the change in noise level. The estimation of the noise level is indeed used for determining the mode likelihood and could thus affect the mode estimation quality.

This study offers an elegant approach for the processing of ECG signal in presence of pathological arrhythmias.

Acknowledgements

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What is claimed:

1. A method for reducing an artifact from a biomedical signal acquired in a noisy environment comprising:
acquiring a first biomedical signal apart from the noisy environment;
modeling the first biomedical signal;
acquiring a second biomedical signal of the same type but acquired in the noisy environment, the second biomedical signal including the artifact;
modeling the second biomedical signal; and
filtering the biomedical signal by determining an estimated signal from a combination of the modeled first and second biomedical signals and then separating the estimated combination of the first and second biomedical signals into an estimated first biomedical signal and an estimated second biomedical signal.
2. The method according to claim 1, wherein the biomedical signal is selected from one or more of an electrocardiogram (ECG), electroencephalogram (EEG), electromyogram (EMG), fetal ECG, blood pressure waveform or photoplethysmograph (PPG).
3. The method according to claim 1 or 2, wherein the noisy environment is a magnetic resonance imaging (MRI) scanner and the first biomedical signal is acquired outside of the bore of the MRI scanner and the second biomedical signal is acquired inside the bore of the MRI scanner.

4. The method according to any of claims 1-3, wherein the first and second biomedical signals are each modeled as a pseudo periodic signal.
5. The method according to any of the foregoing claims, wherein the first and second biomedical signals are modeled by fitting Gaussian parameters to the biomedical signals.
6. The method according to any of the foregoing claims, wherein the second biomedical signal is modeled as a pseudo periodical signal with a periodicity being the same as the first biomedical signal.
7. The method of claim 5, wherein the periodicity of the second biomedical signal is approximated by a sum of Gaussians.
8. The method of claim 1, wherein the second biomedical signal is modeled by solving Navier Stokes equations for different sections of an aortic arch of a subject and by propagating the resulting current source to the torso of the subject.
9. The method of claim 1, wherein the second biomedical signal is modeled in accordance with a polynomial function, a spline function or a function like $f(t) = A \exp(-B(t-T_k)\sin(2\pi (t-T_k)/(T_{k+1} - T_k)))$, T_k being the time of the k th R peaks and $T_k < t < T_{k+1}$ and A B being the parameters of this model.

10. The method of any of the foregoing claims, further including the step of tracking the estimated first and second biomedical signals for abnormalities in the biomedical signal appearing as deviations from the estimated signals.
11. The method of any of the foregoing claims, wherein the filtering involves non-linear Bayesian filtering.
12. The method of any of the foregoing claims, wherein the filtering includes Kalman filtering, particle filtering or Gaussian processes
13. The method of any of the foregoing claims, wherein the filtering step includes use of the following observation equations that provide an estimation of a periodic artifact to be reduced or separated from the biomedical signal:

$$\begin{cases} \varphi_k = \theta_k + v_{1,k} \\ s_k = P_k + QRS_k + T_k + MHD_k + v_{2,k} \\ s_k = MHD_k + \sum_i \alpha_i^{ECG} \exp\left(-\frac{\Delta\theta_{i,k-1}^{ECG^2}}{2b_i^{ECG^2}}\right) + v_{3,k} \end{cases} \quad (3)$$

14. The method of any of the foregoing claims: wherein the artifact is a magnetohydrodynamic (MHD) effect from an electrocardiogram (ECG) signal acquiring during a magnetic resonance imaging (MRI) technique; and wherein the first biomedical signal acquired is an ECG, the second biomedical signal acquired is also an ECG, the modeling of the second biomedical signal includes modeling for MHD effect, and the filtering includes determining an estimated signal from the combination of the modeled first ECG signal and the modeled second ECG signal modeled for MHD effect and then separating the estimated combination of the first and second ECG signals into an estimated ECG signal and an estimated MHD signal.
15. The method of any of the foregoing claims, wherein the filtering involves use of signal quality indices to automatically adjust the observation covariance noise matrix for Bayesian filtering.
16. The method of any of the foregoing claims, wherein the filtering involves use of a multiple model approach and a switching Kalman Filter to allow estimation of the different parameters for the models and selection of the best model.
17. The method of any of the foregoing claims further including outputting the filtered biomedical signal, and wherein the method is a computer implemented method.

18. A computer readable medium executable on a computer for at least one of filtering, segmenting and classifying a biomedical signal including an artifact acquired in a noisy environment, the computer readable medium executing the steps of:
- acquiring a first biomedical signal apart from the noisy environment;
 - modeling the first biomedical signal;
 - acquiring a second biomedical signal of the same type but acquired in the noisy environment, the second biomedical signal including the artifact;
 - modeling the second biomedical signal; and
 - filtering the biomedical signal by determining an estimated signal from a combination of the modeled first and second biomedical signals and then separating the estimated combination of the first and second biomedical signals into an estimated first biomedical signal and an estimated second biomedical signal.
19. A system for reducing an artifact from a biomedical signal acquired in a noisy environment, comprising:
- a data acquisition system configured to acquire a first biomedical signal apart from the noisy environment, and to acquire a second biomedical signal of the same type but acquired in the noisy environment, the second biomedical signal including the artifact; and
 - a processing system coupled to the data acquisition system, the processing system being configured to model the first biomedical signal, to model the second biomedical signal, and to filter the biomedical signal by determining an estimated signal from a combination of the modeled first and second biomedical signals and then separating

the estimated combination of the first and second biomedical signals into an estimated first biomedical signal and an estimated second biomedical signal.

20. The system of claim 19, the processing system comprising:

a local interface; and

a processor, memory, a user interface, and an I/O device, each coupled to the local interface.

21. The system of claim 19 or 20, the processing system comprising a mobile application for a mobile device.

22. The system of claim any one of claims 19-21, the data acquisition system and the processing system being integrated into a single device, or residing on separate devices.

23. The system of any of claims 19-22, wherein the system is a computer system.

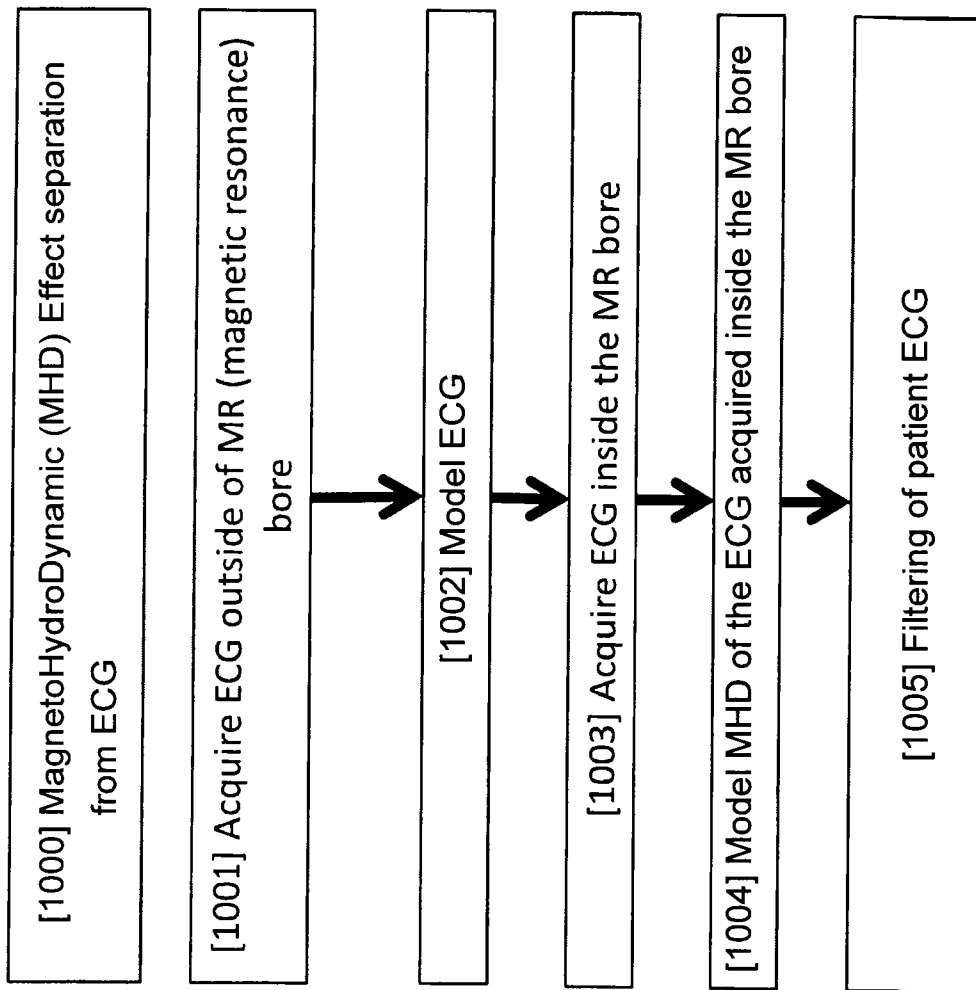


FIG. 1

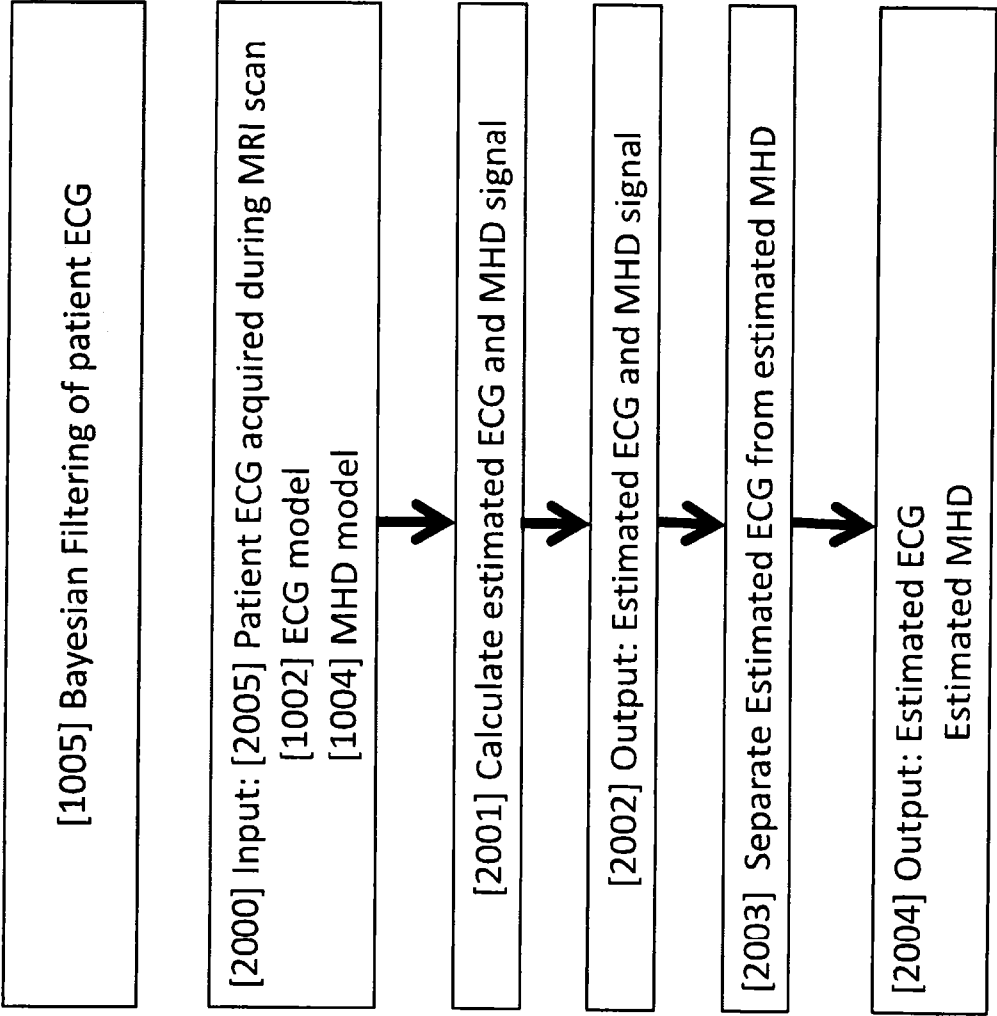


FIG. 2A

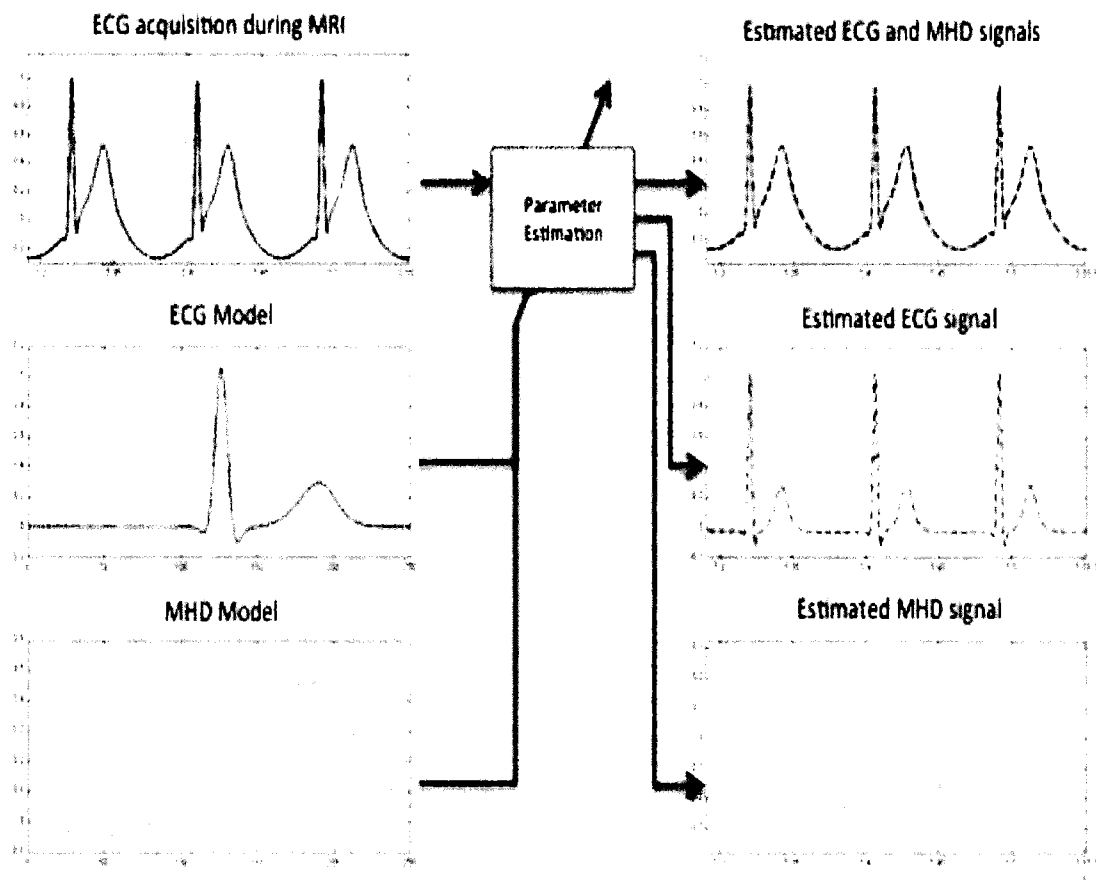


FIG. 2B

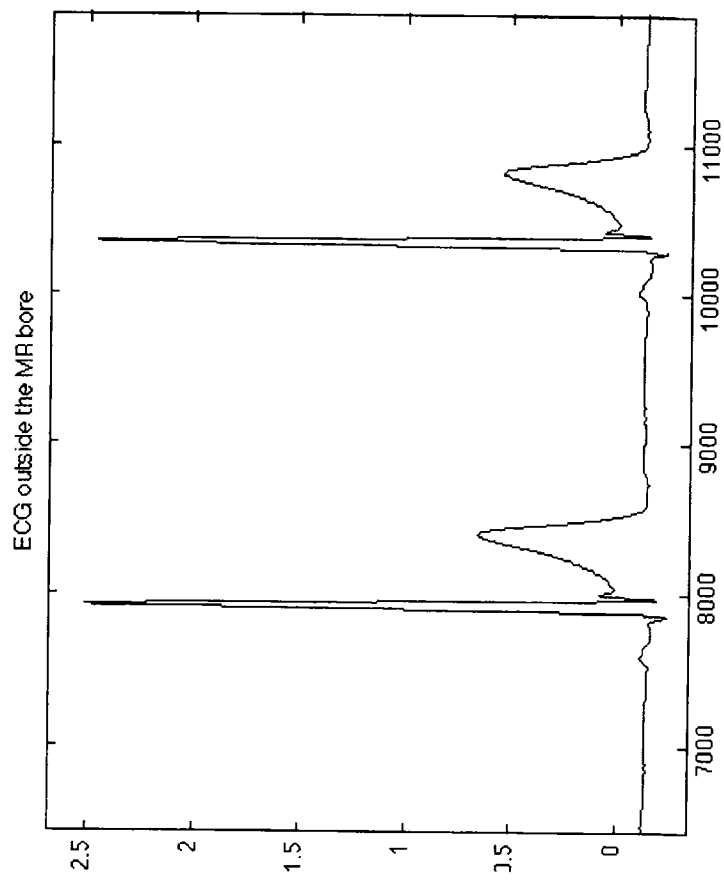


FIG. 3

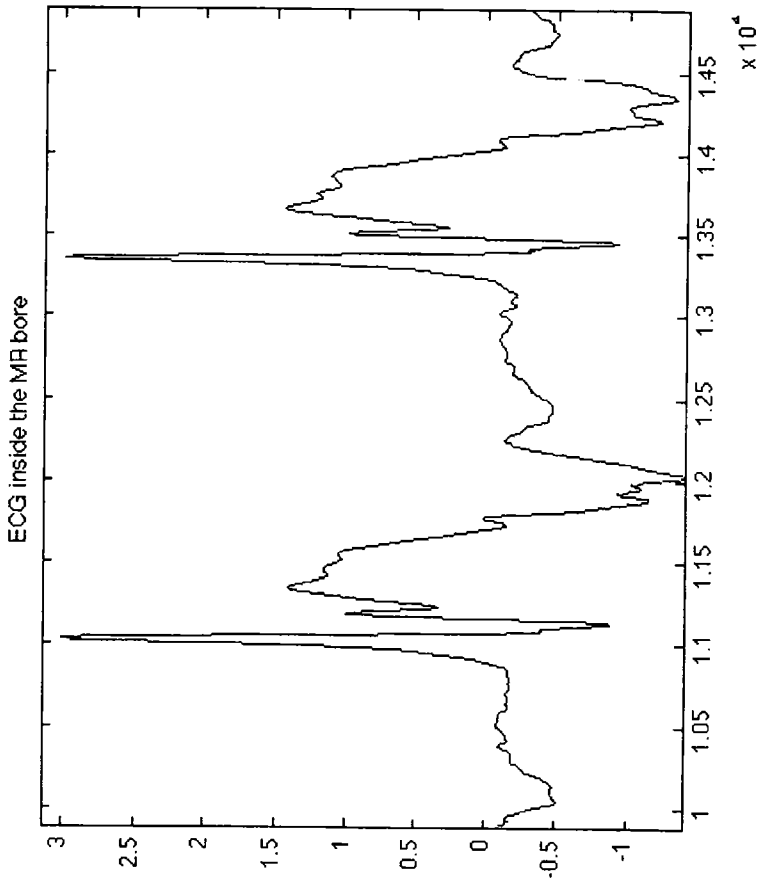


FIG. 4

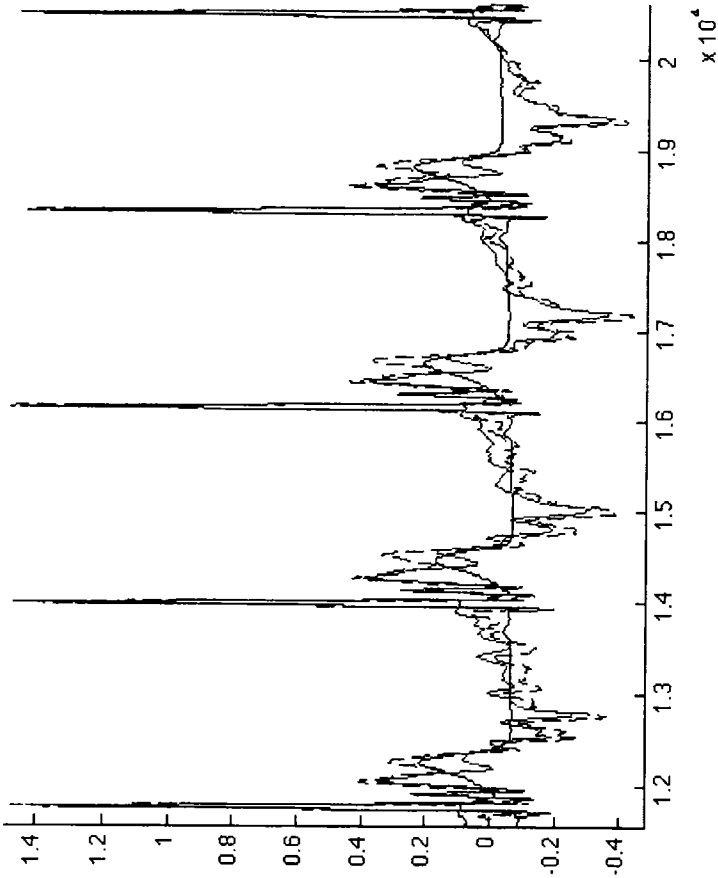


FIG. 5

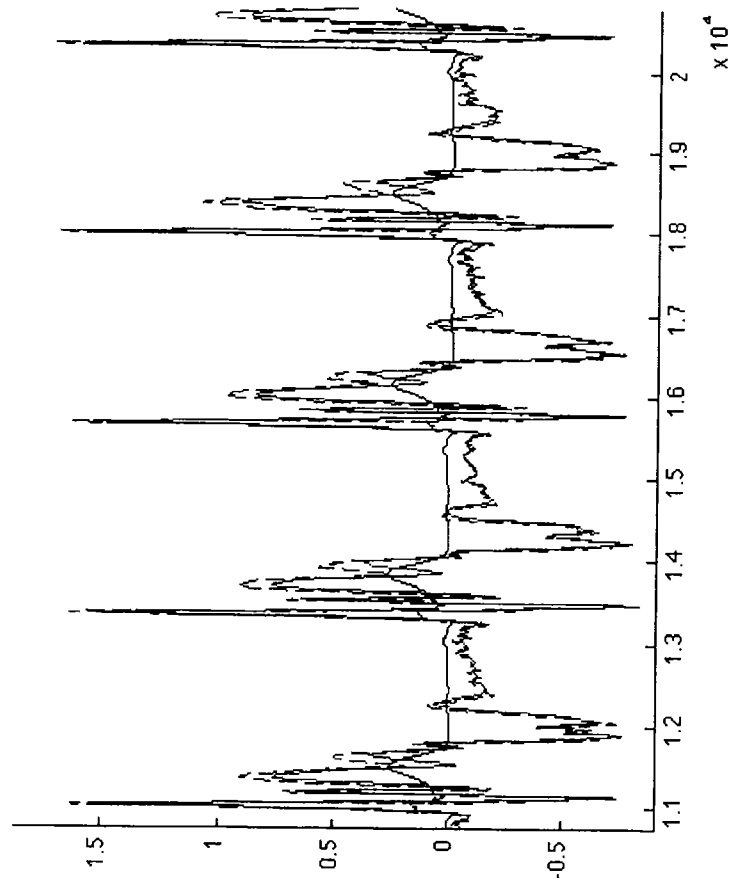


FIG. 6

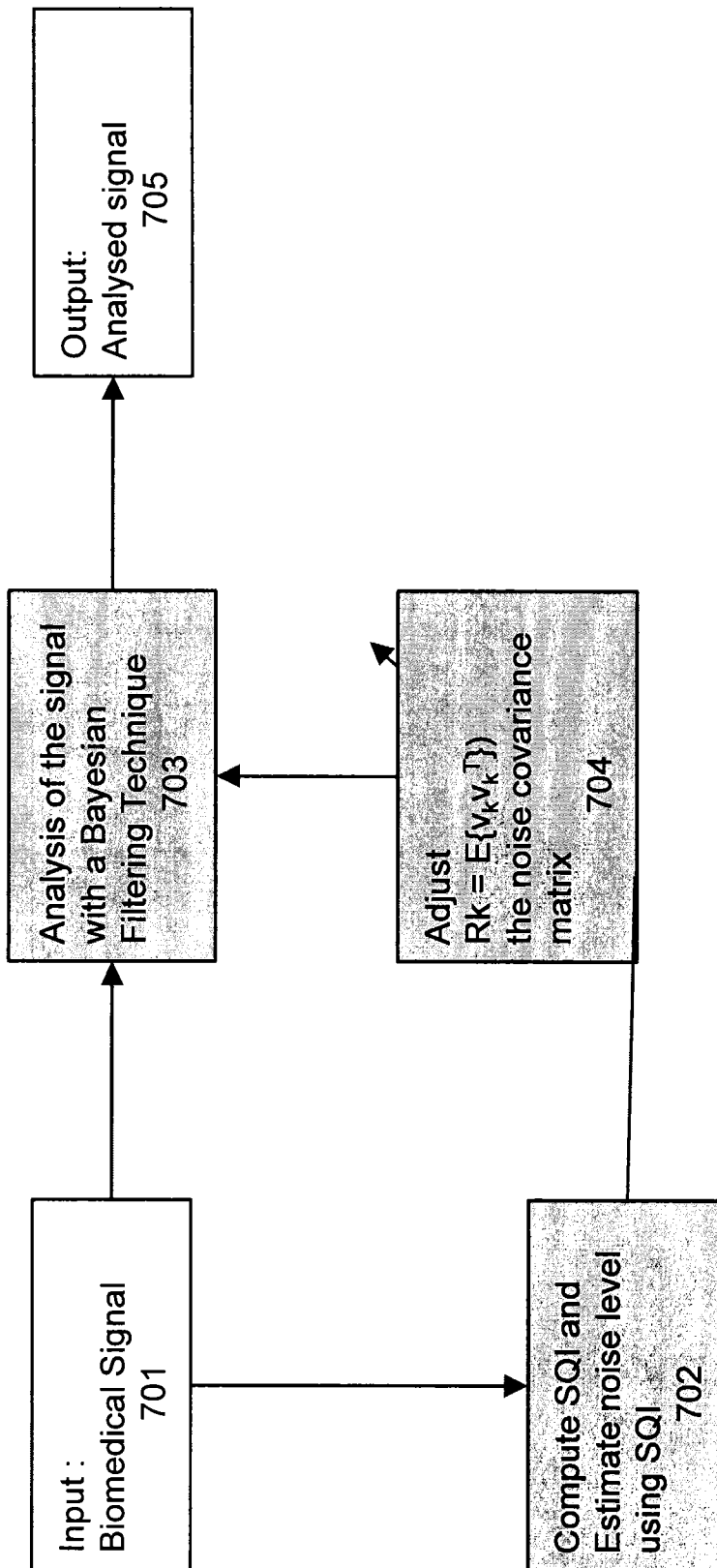


FIG. 7

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US12/59217

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/04 (2012.01)

USPC - 600/513, 508, 301, 481, 300, 509; 702/19, 1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8): A61B 5/04 (2012.01)

USPC: 600/513, 508, 301, 481, 300, 509; 702/19, 1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google/GoogleScholar, IP.com, PubMed: MRI, ECG, EMG, EEG, artifact, navier, mobile, wireless

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 2008/0004537 A1 (UUTELA K) January 3, 2008, paragraphs [0007], [0046] and [0056]-[0058]	1, 2, 3/1, 3/2, 18-20 ----- 8, 9, 21/19, 21/20
Y	US 7272265 B2 (KOURI, D et al.) column 1, lines 38-46, 56-64, column 125, lines 48-51	8, 9
Y	US 2004/0056103 A1 (SEPONEN R) March 25, 2004, paragraphs [0051, 0063], claim 16	21/19, 21/20

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

27 November 2012 (27.11.2012)

Date of mailing of the international search report

04 JAN 2013

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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Facsimile No. 571-273-3201

Authorized officer:

Shane Thomas

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PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US12/59217

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 4-7, 10-17, 22 and 23
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.