1. <Title name>
   1. Analysis of physiological aspects of fetal ECG

Heart defects are among the most common birth defects and the leading cause of birth defect-related deaths. Every year, about one of 125 babies are born with some form of congenital heart defects. The defect may be so slight that the baby appears healthy for many years after birth, or so severe that its life is in immediate danger. Congenital heart defects originate in early stages of pregnancy when the heart is forming and they can affect any of the parts or functions of the heart. Cardiac anomalies may occur due to a genetic syndrome, inherited disorder, or environmental factors such as infections or drug misuse [1].

There are at least two ways of fECG assessment. The key features in are FHR rhythm-related, and FECG morphology related. The second one includes changes in ST and QT segments. It is known that QT interval reacts to situations of stress and exercise. It has been shown that a significant shortening of the QT interval was associated with intrapartum hypoxia irrespectively of changes in FHR [2], whereas in normal labor these changes do not occur.

However, for fECG recordings, it is unclear how robust these measures are, particularly when accompanied by:

* noise/artefacts;
* fetal movements;
* different electrode configurations;
* undesired distortions caused by extraction algorithms.

Moreover, even when using modern monitoring equipment like STAN [3], it is not possible to assess how well the morphology of the fetal signal is preserved. This because the reference (invasive FECG) is based on a different lead, which represents another projection of the cardiac electrical activity.

* + 1. Fetal QT interval feature

A small number of researches conducted on the association between the fetal QT interval and newborn outcome. Although, many studies note QT interval abnormalities during the fetal and newborn period with serious events, including sudden death [4].

A prolonged QT interval, either genetic or acquired, predisposes to ventricular tachycardia and sudden death. Changes in the QT interval have also been shown during exercise, stress, infection and heart failure [5]. A QT shortening was noticed in conjunction with an increase in T-wave amplitude. It seemed logical to assume that the QT shortening would depend on the ability of the fetal myocardium to enhance its performance in response to a catecholamine surge and on h-receptor activation known to elicit the rise in T-wave amplitude.

* + 1. Fetal ST interval feature

The ST interval comprises the ST segment and the T wave, and both relate to the repolarization of myocardial cells in preparation for the next contraction, an energy-intensive process. An increase in T-wave height (fig. 1), quantified by the T/QRS ratio, occurs when cellular energy production within myocardial cells begins to decline, that is, when the oxygen supply is inadequate to maintain metabolic activity so that cells are forced to generate energy by ß-adrenoceptor-mediated anaerobic breakdown of glycogen reserves.

ST interval depression indicates an imbalance between the endocardium and epicardium because of the difference between the lower blood perfusion pressure of the endocardium and the higher mechanical strain, which delays myocardial repolarization.



Figure 1. Changes in fetal ST segment

All the factors that modify the performance characteristics of the myocardial wall, including hypoxia, prematurity, infections, maternal fever, myocardial dystrophy, maternal diabetes and cardiac malformations may depress the ST interval.

* + 1. Fetal heart rate

The basic premise underlying FHR as a tool is that patterns reflect the oxygen status of the fetal brain. The changes and patterns seen in the FHR in response to changes in oxygenation and acid/base status should be considered as the fetal organism attempting to maintain homeostasis [7].

There are both accelerations and decelerations exist in the life of fetus. The first ones appear as exposure to external influence such as tactile or acoustic actions. In addition, accelerations could be served as a manifestation of short spontaneous increase in sympathetic activity. The presence of heart boosts indicates the absence of severe hypoxia or acidosis. However, accelerations may not be appeared in different cases, during fetal sleep, arrhythmia, exposure to certain medications, and extreme prematurity.

Decelerations usually serve as an alarm indicator depending on the temporal relationship to contraction. They can be early, late, variable or prolonged. Early decelerations remain the state without certain mechanism description. They appear quite rare and do not serve as a decease alarm.

One of the mechanisms of variable deceleration is a compression in umbilical cord. At first, as an exposure on decreased blood flow heart becomes beating more often. Further cord compression leads to occlusion of both the umbilical vein and arteries, leading to a marked increase in peripheral vascular resistance and a resulting abrupt decrease in the heart rate. However, another mechanism, which shows deceleration/acceleration, exists [7]. Late decelerations are most consistently associated with a response to a reduction in fetal oxygenation. The normal fetus will tolerate this brief reduction well. In contrast, when oxygen tension is already low, the loss of oxygen tension leads to vasoconstriction. Baroreceptors recognize this increase in fetal blood pressure and instigate a lowering of the FHR.

The final type of deceleration is the prolonged deceleration, defined as more than 2 minutes in duration but less than 10. The most likely mechanism in this type of deceleration is a sudden and prolonged reduction in oxygen delivery. Experts speculate that the decrease in FHR is an attempt to conserve oxygen in cases of severe debt. Thus, such type of deceleration became the brightest in problem indication.

* 1. Methods for registration fetal heart activity

Electronic fetal monitoring techniques can be invasive or non-invasive with intermittent or continuous assessment; these techniques include fetal phonocardiography, Doppler ultrasound, cardiotocography, fetal magnetocardiography and fetal electrocardiography [8].

Cardiotocography is a technical means of recording the fetal heartbeat and the uterine contractions during pregnancy. It uses both ultrasonic measurement sensor for fetal heart rate and electrodes for uterine contractions. However, cardiotocography may also include fetal activity measurement devices [9]. All the transducers

* + 1. Magnetocardiography

Fetal magnetocardiography, the magnetic analog of fetal ECG, is an emerging technology that is uniquely suited for investigation of fetal cardiac electrophysiology. Owing to its ability to assess fetal heart rate, rhythm, and conduction with efficacy similar to that of postnatal ECG.

Despite its advantages, fetal MCG is not widely used. A major barrier to clinical adoption is the high cost and complexity of Superconducting Quantum Interference Device technology. However, recent researches changed the situation. The demonstration of a new type of optically pumped magnetometer (OPM) can achieve SQUID sensitivity in a room temperature device [10], and thus, be a much cheaper and simpler in use method for fetal MCG acquisition. Signals obtained by both acquisition methods are presented in figure 2.



Figure 2. Fetal magnetocardiography with different acquisition methods

Characterization of normal fetal behavior is fundamental to neurodevelopmental research and to clinical fetal evaluation. The compromised fetus restricts its activity [11]. Fetal magnetocardiography allows FHR extraction, fetal heart activity assessment and its own morphology evaluation. Figure 3 presents changes in fetal magnetocardiography during gestation.



Figure 3. Fetal magnetocardiography during gestation

Magnetocardiography morphology and amplitude difference is clearly seen between ages, so it has a real potential in future investigations with more advanced and apparently cheap sensors.

* + 1. Fetal electrocardiography

Two methods of fetal electrocardiogram acquisition exist: invasive and non-invasive. First one includes scalp electrode to obtain direct contact with fetus body. This way provides quite clear signal without any significant interference. However, baseline drift, electrode contact noise, electronic noises, power interference and movements with uterine present in signal [12].

Non-invasive fECG technic means abdominal acquisition method, where in mess of signals fetal cardiogram exists and can be extracted with powerful processing methods.

In general, abdominal fetal acquisition system present following modules:

* Acquiring module.
* Signal preprocessing module
* Transducing module.
* Signal processing and Analysis module.
* Data performing module.

However, actual problem is located in theoretical knowledge about data processing and analysis, module placement. Approximate structure contains of microcontroller as the overall module for signal preprocessing and transducing and others that shown in figure 1.



Figure 4. Fetal ECG monitoring system

In addition, usually fetal monitoring systems includes more lead with other different purposes, for example, myographic measurements such as uterine contractions and channels for amplified mother ECG. They can be used for feature extraction and analyzing methods as well as alarm indicators.

* 1. Instrumental methods for fECG registration

The most frequently used fetal monitoring technology uses a Doppler ultrasound device to obtain fetal cardiac activity, either the fetal heart itself or arterial flow through a major fetal vessel. An algorithm in the device calculates the time interval between the loudest points in the cardiac cycle and displays a heart rate. Fetal electro cardio signals are much harder to obtain clearly and analyses, thus, in many cases only fetal heart rate measurement is used.

Nevertheless, the majority of attempts keep stepping on the road of technology and methodology improvement. Several monitors and remote biomedical devices for fetal heart rate or ECG waveform acquirement are used widely.

* + 1. Monica AN24

The first FHR monitor using noninvasive fetal ECG technology to arrive in the American clinic was the Monica AN24 monitor. It collects fetal ECG data from five electrodes placed on the laboring woman’s abdomen. The technical challenge for the Monica AN24 and other similar monitors is that, at the point where the electrodes are placed on the maternal abdomen, the fetal ECG waveform is overwhelmed by the maternal ECG, which has a voltage 100 times greater than its tiny fetal counterpart [13].

Monica AN24 is able to obtain 4 channels with 5 electrodes where one common is placed on the referenced point, usually close to the back. The main unit uses advanced technics to extract MHR, FHR and uterine activity. And thus, there is no way to present fetal or mother ECG itself. The device is presented in figure 3.



Figure 5. Monica AN24

In addition, researches proved supremacy of use Monica AN24 over basic CTG technics for obtaining fetal heart rate and uterine contractions. Moreover, woman with big Body Mass Index raises difference in result with the use of electrodes and ultrasound sensors, that has been shown in [14, 15].

* + 1. Monica Novii

Monica Novii is a device developed to improve the labor and birthing experience with remote monitoring. Wireless Patch System is an intrapartum fetal monitor that non-invasively measures and displays the FHR, maternal heart rate, and uterine activity with only five electrodes that communicate all maternal and fetal information to the Novii Pad through Bluetooth technology. The device detects the fetal ECG and maternal ECG rather than FHR through Doppler on a separate device when using standard EFM [16].

For contractions, the Novii uses electromyogram signals from the uterine muscle to detect uterine activity rather than external tocometry. The suggested benefits of this device include reliable tracing on high body mass index patients and patient comfort as the user has a wireless experience during labor and child birth which can increase satisfaction for those who desire frequent position changes and movement [17].



Figure 6. Monica Novii patch system with interface

Despite the fact that monitor provides FHR and MHR it doesn’t use any complex techniques for fetal ECG morphological analysis. However, there is a possibility to show signals from Novii pod.

The Novii Interface is an accessory to the Novii Pod which provides a means of interfacing the wireless output of the Novii Pod to the transducer inputs of a CTG Fetal monitor. The Novii Interface enables signals collected by the Novii Pod to be printed and displayed on a CTG Fetal Monitor and sent on to a central network, if connected [18].

Novii pod system with patches contains 5 electrodes that is shown in figure 5. The positioning of electrodes has been chosen that way to amplify their individual signals. Thus, electrode 4 is implied as neutral one; 3rd significantly important for detection of uterine contractions. Second one for mother’s ECG, it places in the closest location to mothers’ heart among others. Electrode number gives significant contribution to fetal ECG analysis, and thus, FHR extraction.



Figure 7. Novii pod system

One significant contraindication exists Monica Novii is used only with woman over 36 completed weeks of pregnancy. That is usually the last month of gestation.

* + 1. Meridian M110

Meridian system includes monitor and electrode patch. In my opinion, the most significant advantage of a patch is focused in usability comfort. The Meridian Electrode Patch eliminates the need for skin preparation and replaces the fetal scalp electrode, intrauterine pressure catheter, Doppler, and TOCO sensors with a single non-invasive disposable system, while maintaining the same accuracy and sensitivity performance expected of today’s monitoring devices.

Meridian M110 Electrode Patch consists of four patches (fig 6), two for the mother’s abdomen and one for each of her sides, which provides continuous fetal ECG signal pick up for any fetal position or movement [19].



Figure 8. Mindchild Meridian electrode patch

Meridian monitor is a main computational unit for channel processing and indicators extraction. Market has small number of devices for fetal monitoring, however, all of them have personal unique features. Current device is considered to be the one which can perform well for woman with obesity.

MERIDIAN M110 is the only fetal monitor on the market that performs as well in obese patients as it does in lean patients. Both the fetal heart rate signal and the contraction signal deteriorate when BMI increases, compromising obstetric safety [20].



Figure 9. Mindchild Meridian monitor

Moreover, The Meridian M110 demonstrated in a clinical trial: 96.7% correct fetal heart rate as compared to the fetal scalp electrode; 98.0% agreement of a contraction event as compared to the intrauterine pressure catheter and 98.3% correct maternal heart rate as compared to the pulse oximeter.

* + 1. Patents for fetal ECG acquisition systems

There are a lot of fetal monitoring devices exists, however, only a few of them are considered to be reliable, robust and standard. Nowadays, public market mostly includes devices for FHR assessment with ultrasound principle of operation. But, other medical inventory is still slowly filling the market, replacing outdated samples.

First system is described in [11], it contains of 3 electrodes and measurable unit with display. Electrode displacement allows the extraction of fetal heart rate and mothers heart rate from abdominal signals. One of wires are connected two the back, where signals are less seemed to be mixed.

The structure of main unit is pretty simple. Signals from leads had to be preprocessed. Then, mothers and fetal contents are derived from the mixed signal and analyzed to retrieve following indicators, their heart rates.

In addition to display block, device also has storage to save final result and preprocessed data for future outer analysis. There is more than one device version, it differs in number of leads. However, an average result for abd2012 database in most of channels seems great (F1 score > 94%)

Another device that is described in [22] has the similar architecture except. Initial device purpose is a prevention of respiratory disease outcomes from abdominal signals. It can measure a bunch of parameters, from mother/fetus physical activity to both ECGs.

The main distinctive feature of this system is an integration of several units in one complex sensor environment. Units can be mounted in some ways: with adhesive, tape. In addition, garments with sensors within are used for special conditions.

* 1. Algorithmic methods for fECG evaluation

After extracting the fECG from maternal abdominal recordings, the next step is to extract clinical parameters from the fECG. Adult ECG is different in SNR from fetal one. Thus, some improved techniques are used for signal enchasing, feature extraction and analysis.

Nowadays, the most common feature for fetal health evaluation is FHR. However, there are some important morphological metrics physiologically described in previous subchapters. Several advanced and not so techniques are presented in following subchapters.

* + 1. Fetal heart rate extraction and analysis

It is important to note that most techniques for FHR extraction contains additional part of fECG extraction from abdominal signals. The main idea of rate obtaining is to find locations of R-peaks; however, signal appearance can be performed in different unrecognizable ways.

Classical R-peak detection methods such as local peak search and the Pan-Tompkins method can be used for both adult and fetal R-peak detection. However, due to the lower SNR of the fetal ECG component improved methods used. The one described in [23].

Proposed R-peak algorithm is divided in stages, that are presented in figure 8. In the first stage, the selected fECG component is passed through a matched filter with a narrow fetal QRS template (of width b1) used as its impulse response. The template can be selected from the data by visual inspection, or as proposed in [24], by using predefined fixed QRS-like functions.

The output is squared and time-averaged with a moving average window of length w1, to obtain the energy envelope. The same procedure is repeated by using a wider fetal ECG template containing the entire PT-interval with a length b2 more than b1, followed by squaring and temporal averaging with window length w2 more than w1.

While, the first stage detects sharp QRS— and QRS-like— peaks of the signal, the second stage targets wider events. Right after the compensation of the group delays of the moving average filters and multiplying the two energy envelopes, the local peaks of this product can be considered as the fetal R-peaks.

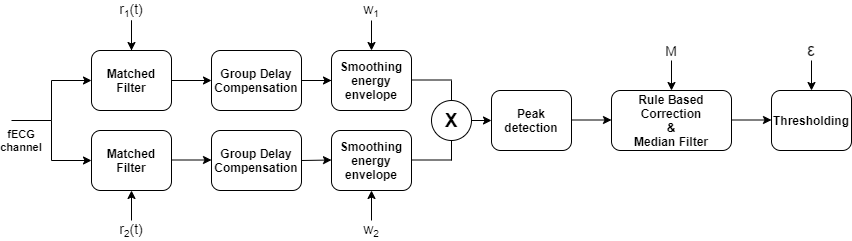


Figure 10. Double matched filter R-peak detection scheme

Having detected the fetal R-peaks, in order to refine the calculated heart rate time series and the excess or missing R-peaks, a rule-based correction and conditional median filter is applied as post processing, which corrects the outlier R-peaks, while keeping the normal beats unchanged.

Another approach is described in [25], author uses empirical mode decomposition. More specifically, they assess different EMD technologies for channel selection. EMD is a fully data-driven method for non-linear and nonstationary real-world signals; it decomposes a signal into a finite set of intrinsic mode functions that represent its inherent oscillatory modes. However, R peaks are extracted with wavelet coefficients both for mother and fetus out of noise signals.

There is a standard for evaluation of fetal heart tracings; it emphasizes following parameters and patterns:

* Baseline
* Baseline variability
* Early decelerations
* Variable decelerations
* Late Decelerations

Different techniques are used for health evaluation with FHR, it is important to admit, that uterine contraction event is a significant time point for observation the changes of FHR. However, UA has low frequency, thus, FHR tracings should be quite long in time, hence, it is a rough task to obtain enough amount of clean data for right assessment.

Ones were using FHR for predicting fetal acidemia. They used useful approach with convolutional neural network (CNN) [26]. Actually, CNNs in their structure take some n-dimensional signal as input and underline useful features by itself. Another, important step they’ve done was transferring FHR curve to 2D form with continues wavelet transform (CFT) which also reflects time and frequency features in a single signal. In conclusion, the average accuracy achieved is 98% with area under ROC about 97%, that is explicit success.

Another useful review presented open access software for detection anxious fetal state [27]. Group used a bunch of parameters that a shown in figure 9 as features for training different classifiers. Predictive value was the absence a fetal distress, however, they estimated if cord artery pH more less than 7.2 or not.

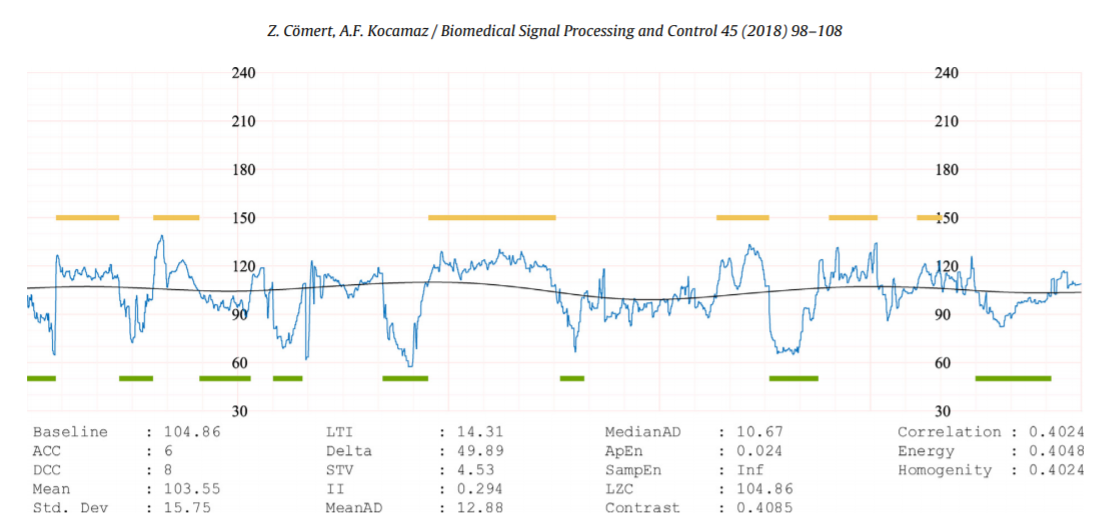


Figure 11. Analysis report produced by CTG-OAS

Features can be divided in 4 groups:

* Morphological (up to DCC)
* Linear (up to MedianAD)
* Non-linear (up to LZC)
* Image-based time-frequency

Authors investigated 3 classifiers: Support vector machine, k nearest neighbours and artificial neural network (presumably n-Dense layers NN). Results were presented in different parameters; however, actual performance is evaluated by AUC, which SVM has about 84% (98% max, 68% min). Much more studies reviewed the use of CTG-OAS with different datasets; some of them are private. But outcome is poor, as for assessment parameter geometric mean of sensitivity and specificity all values are about 80%.

* + 1. Morphological analysis

Entire morphological analysis is built on the ECG segments, which include amplitudes and intervals. Thus, while the first step of FHR based methods was the detection of time location of R-peaks, segments requires higher level of algorithms to be received that makes this field is extremely tough to be pushed forward. Elimination of noises and artifacts becomes one of the most important tasks for data analysis with successful outcome.

Researchers have extracted parameters such as the QT-interval and the ST-segment. The typical benchmark for these studies is commonly the invasive fECG obtained from the fetal scalp electrodes acquired during labor. Furthermore, it is currently difficult to evaluate the fECG parameters independently since there are very few open-access fECG databases with expert annotations.

Early attempts of the extraction a fetal ECG from abdominal signals were proposed in previous decade, one used Bayesian filtering neural network for morphological features extraction in [2]. A Bayesian Filtering Framework based on an Extended Kalman Filter for extracting the FECG from a single abdominal channel was used with training database of 20 one minute maternal-fetal mixtures and evaluated on 200, one-minute mixtures. A single pass of the EKF was performed to cancel out the maternal ECG in order to build an average FECG morphology. A dual EKF was then applied to separate the three sources present in the signal mixture.

Another recent approach is presented in [28], they use LSTM network with different structure. The main feature of the is covered under “Fast” LSTM cell in architecture. The architecture of LSTM was originally designed for long term dependencies in data sequences, such as speech recognition and machine translation, which frequently utilize the dependencies between words with long word span.

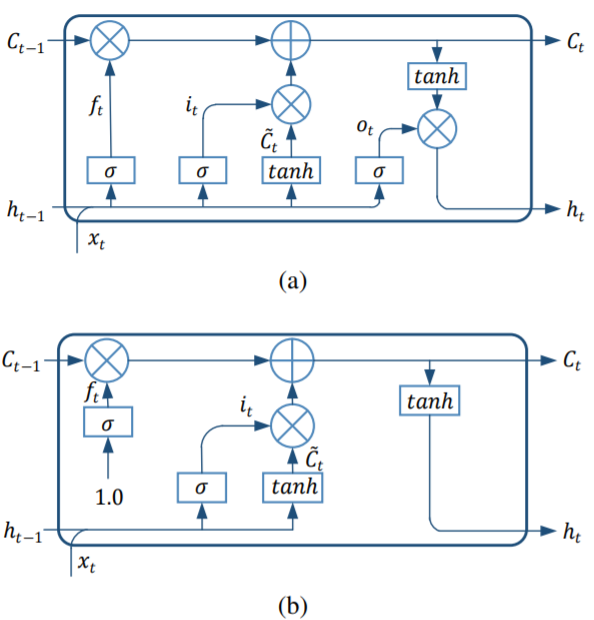


Figure. 12 Architecture comparisons of cell units. (a) The original architecture of LSTM; (b) The proposed architecture of the fast LSTM.

However, the internal mapping system of the FECG signals is causal and locally consistent on the timeline. Thus, the attenuation coefficient of the hidden state should be smoothly variant or constant, which is different from the mechanism controlled by the original forget gate.

More concretely, the forget gate is switched to a relatively constant value, which obtains the gate value without taking xt and ht as input. They also abandoned the output gate, since they found that the output gate has little effect on the function of LSTM in the FECG enhancement stage, which has also been proved in other applications [29]. The definition of the input gate is kept intact to maintain the function and flexibility of LSTM. The architecture of the fast LSTM is shown in Figure 2b.

For evaluation purposes they used two datasets: Database for the Identification of Systems (‘DaISy’, 1987) [30] and Fetal ECG Synthetic Database (‘FECGSYNDB’, 2016) [31]. Real data don’t have fECG separated signal, thus, it was used for quantitative evaluation, while DaISy was used for qualitive evaluation in comparison with other methods.

Slow-fast LSTM achieves higher means of SNR (about ~8 with high 12dB noise), and smaller standard deviations indicating the highly adaptive ability. Other channels with mean are presented in Table 1.

Table 1. SNRout of Methods on Records from FECGSYNDB

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| SNR | C0 | C1 | C2 | C3 | C4 | C5 | Mean ± Std. |
| 00 | 2.84 | 6.07 | 5.33 | 3.61 | 6.01 | 5.02 | 4.81 ± 1.20 |
| 03 | 6.67 | 5.76 | 5.99 | 5.46 | 6.19 | 6.03 | 6.02 ± 0.38 |
| 06 | 5.93 | 7.94 | 6.11 | 4.94 | 8.49 | 5.80 | 6.54 ± 1.25 |
| 09 | 7.78 | 8.95 | 9.09 | 6.67 | 9.13 | 8.01 | 8.27 ± 0.89 |
| 12 | 8.48 | 9.45 | 10.34 | 8.34 | 8.73 | 9.75 | 9.18 ± 0.73 |

Qualitative outcome is shown in figure 10, waveform seems to be more accurate than other methods. However, FastICA algorithm provided successful outcome in some channels as well as ESN.

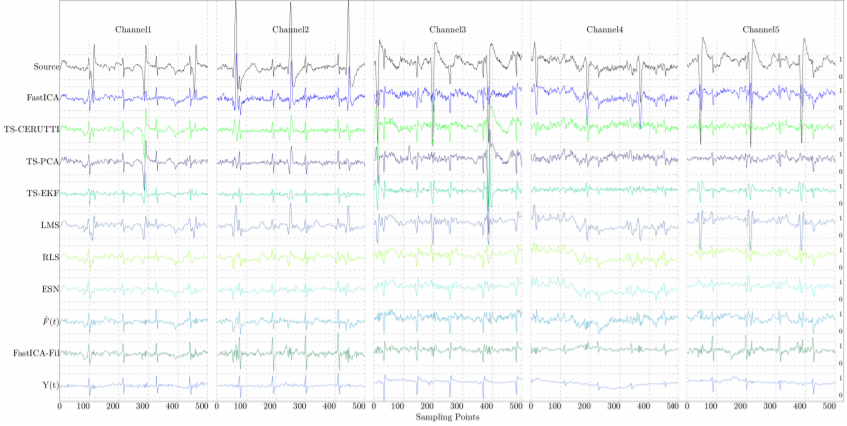


Figure 13. SFLSTM outcome Y(t) in comparison with other methods, all outputs are normalized by the same certain value.

Finally, to date, morphological features are not used in the field of NI-FECG because todays algorithms do not provide required signal quality and medical fundamentals are not ready yet.

* 1. Setting goals and objectives

Fetal Heart Rate (FHR) monitoring based on the analysis of the fetal heart rate signal is the most common method of medical assessment of fetal condition during pregnancy. Visual analysis of FHR signals demonstrates a challenge due to the complicated shape of the waveforms [32].

Thus, computer-aided fetal monitoring systems provide a number of parameters that are the result of the measurable investigation of the registered signals. These parameters are the basis for a qualitative analysis of the fetal instant condition. The methods for the interpretation of FHR values provided by a Doppler device are commonly used in clinics for determining the fetal’s condition: died in the womb, caesarean section is needed or normally progressing.

Another way of fetal ECG assessment is morphological analysis, but todays researches are still should be investigated more in the field of clean ECG extraction and the whole methodology creation. Thus, it is not used in current master’s thesis.

However, the idea of searching the presence or absence of fetus’s critical conditions with FHR requires several steps to be done:

* Preprocessing abdominal ECG
* Fetal ECG extraction
* FHR calculation
* FHR analysis.