

## Mathematical tools for identifying the fetal response to physical exercise during pregnancy

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### 1 Physical exercise and pregnancy

As physical exercise has become part of everyday life, it is natural that most of the women that become pregnant wish to continue their exercise routine. It is, however, very important to obtain information regarding the effects of exercise during pregnancy regarding both fetal and maternal anatomy and physiology in order to avoid any possible negative effects on the fetus [3].

In the applied mathematics literature there exist a significant number of tools that can reveal the interaction between mother and fetus during rest and also during and after exercise. These tools are based on techniques from a number of areas such as signal processing, time series analysis, neural networks, heart rate variability (see section 3) as well as dynamical systems and chaos (see section 4). We will briefly review here some of these methods, concentrating on a method of extracting the fetal heart rate from the mixed maternal-fetal heart rate signal, that is based on phase space reconstruction.



Before we describe the mathematical tools that have been developed in order to identify the fetal responses, it is worth having a closer look at the opinion of the physiologists: According to the majority of researchers, a pregnant woman that has no complications regarding her pregnancy can exercise without any maternal or fetal problems [8]. However, the exercise prescriptions during pregnancy are strongly dependent on the different types, different amounts and different intensities of exercise: regarding high intensity exercise, some of the data still lack the statistical power to make definitive statements and recommendations.

In the medical literature there exists a large number of descriptions of the impact of maternal perceptions, sensations and emotions on the fetus. Even though no direct neural connections between mother and fetus exist, it has been found that maternal experiences generate a cascade of physiological and neurochemical consequences that may affect the fetus, either directly or indirectly [17]. Regarding maternal exercise, the existing published data suggest that it may have brief or lasting effects on the fetus [3]. During maternal physical exercise, significant cardiovascular changes occur. The most potentially adverse effects on the fetus come from the fact that the maternal blood is, during exercise, re-distributed away from the splanchnic organs and towards the exercising muscles [3]. Another very important factor is that, during exercise, the body core temperature may increase to levels that could have teratogenic effects [3], especially during the first trimester. It should be noted that this review is specifically on the fetal response to maternal exercise and therefore we do not discuss further the embryonic response to maternal exercise in the first trimester.

The most studied parameter of fetal physiology is the fetal heart rate (*FHR*). In fact, the identification of various fetal heart rate patterns has provided obstetricians with a very valuable tool for assessing fetal well-being. Typical changes in FHR patterns are known to reflect hypoxia or asphyxia, as well as sympathetic and parasympathetic activity [3]. Regarding sustained maternal exercise, it has been shown that the fetus reacts with a moderate increase in baseline heart rate [47]. All studies agree that, in response to maternal physical exercise, the fetal heart rate is elevated from 5 to 25 beats/min, returning to the normal levels 15-20 minutes after the end of the exercise program [8]. Changes in the fetal heart rate during maternal exercise have been reported regarding factors such as movement of the fetus, breathing, fetal temperature or blood uptake in the zone of the uterus. Such responses are not considered to affect the health of the fetus, as long as the



Figure 1: Exercise during pregnancy? Mathematical tools can serve as an aid to reveal the fetal response and identify possible problems.

intensity of the exercise is moderate. Episodes of fetal bradycardia have also been reported; however this is considered to be a normal response which is adapting to the maternal exercise [8]. In general, current research suggests that physical exercise in healthy pregnant women is not a reason for a change in fetal heart rate patterns suggestive of fetal distress. It should be noted however that there is a significant increase in uterine activity during physical exercise [41] which, if excessive, could cause fetal distress.

In the sections that follow we review a number of mathematical methods that have been developed to help monitoring the fetal heart rate response. Such methods serve not only as a research tool but also can be incorporated as a clinical aid for fetal surveillance [3].

## 2 The fetal heart rate and the fetal electrocardiogram

The response of the fetal heart rate to maternal physical exercise has been studied repeatedly. The important question of what is the normal FHR response to maternal exercise, is not easy to answer, because of the many factors that affect it. One of the limitations is that it is difficult to achieve accurate measurements of the FHR during maternal exercise [41]. Another important question is on whether there is any coupling between the fetal and

maternal cardiac systems [46].

Considering how important it is to control the fetal heart rate response, it is not surprising that the extraction of the *fetal electrocardiogram (FECG)* from the maternal electrocardiogram (*ECG*) has become an interesting and challenging problem in biomedical engineering. The extraction of FECG is of vital importance also from a clinical point of view, as it provides information about the health of the fetus.

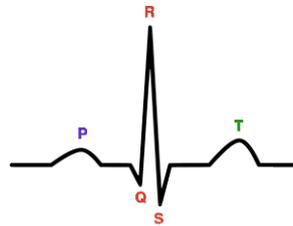


Figure 2: Schematic representation of a normal ECG.

An electrocardiogram is usually obtained through skin electrodes attached to the mother's body. Generally speaking, a human ECG records the electrical activity of the heart over time. As the heart undergoes depolarization and re-polarization, the electrical currents that are generated spread not only within the heart, but also throughout the body. This electrical activity can be measured by a set of electrodes placed on the surface of the body; the resulting recording is the ECG. Figure 2 shows a typical ECG recording consisting of a P wave, a QRS complex and a T wave [18, 48]. The QRS complex is a structure on the ECG that corresponds to the depolarization of the ventricles [48]. It should be noted here that the shape of the QRS complex in figure 2 is idealized. In fact, the shape changes depending on which recording electrodes are being used. The shape will also change when there is abnormal conduction of electrical impulses within the ventricles [18]. The actual value of the heart rate can be calculated from the intervals between the different waves.

The fetal ECG signal is much smaller in amplitude than the maternal ECG signal. Also, under normal conditions, the fetal heart beats faster than the maternal, however, both signals are very similar. Obviously for the acquisition of the FECG, noninvasive techniques are preferred. The desired fetal heart rate signal appearing at the electrode output is however always corrupted by considerable noise: the extremely high amplitude maternal elec-

trocardiogram, the mother's respiration, power line interference, or noise due to electronic equipment [31, 52]. As mentioned before, obtaining an FECG is not an easy task and therefore a number of methods have been proposed to address this very important problem.

### 3 Mathematical techniques for FECG extraction

Figure 3 (published in [36]) shows the maternal ECG, consisting of the ECG signal of both the mother and the fetus. The FECG signal can be observed as small spikes within the maternal ECG [36], surrounded also by experimental noise.

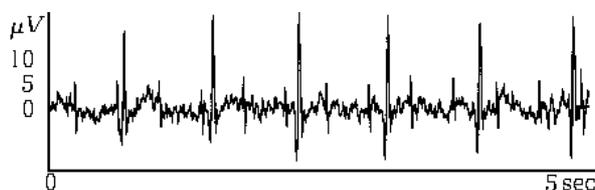


Figure 3: ECG of a pregnant woman including the maternal and fetal heart rate components. Figure printed in [36], page 135.

The aim of the mathematical techniques is to extract the fetal component from a maternal ECG signal such as the one shown in figure 3 and provide a clean FECG time series that can be further analyzed in search for possible abnormalities. The techniques that can be found in the literature are numerous. We will very briefly review in this section the most commonly found ones. Most of these approaches are evaluated using simulated maternal ECG signals or/and a very small data set of real recordings.

To begin with, we note that a significant number of studies found in the literature report the implementation of the *wavelet transform* for the extraction of the fetal heart rate, see for example [27, 42]. In particular, in the work of [42], a wavelet transform is applied in order to extract the wavelet-based features of the fetal cardiac signal so that the normal cases can be easily distinguished from the abnormal ones.

Another method to monitor fetal heart rate patterns is by studying the fetal *heart rate variability*. It has been shown that heart rate variability is an important marker for the fetal well-being [45]. Various methods have been therefore used to analyze the fetal heart rate variability, in particular concerning variables from both the time and the frequency domain [26].

A promising approach is the so-called *blind source separation (BSS)* or independent component analysis [9, 14, 22, 23, 51, 52]. Blind source separation is the separation of a set of signals from a set of mixed signals, without information (or with very little information) about the nature of the signals [49]. The BSS technique separates a set of signals into a set of other signals, assuming that the original signals are non-redundant (for example, the signals may be mutually statistically independent or de-correlated) [49]. It was reported that the results by BSS were more satisfactory than those by classical methods [2, 51]. Separating all of the source signals from a large number of observed signals takes, however, a long time and is often not necessary [52]. A more convenient choice of method could be the *source extraction* method [10, 13, 14, 15, 52], that is closely related to the BSS. The source extraction methods use the basic principles of the BSS methods but make additional use of prior information about the autocorrelation property of the FECG from the noisy free measurements [31].

To finish our brief review on the FECG extraction methods, see also [28, 31], we note below the use in the literature of methods such as:

- *singular value decomposition (SVD)* [24]
- *matched filtering* [34]
- *adaptive neuro-fuzzy inference systems* [4]
- *dynamic neural networks* [12]
- *temporal structure* [10]
- *fuzzy logic* [6]
- *frequency tracking* [11]
- *polynomial networks* [5]
- *multi-reference adaptive noise cancellation* [51]

- *real-time signal processing* [21]
- *time-frequency analysis* [29]

All the above techniques have been successfully applied to the extraction of the fetal cardiac component and the results have been reported satisfactory, either by use of simulated ECG signals or by their implementation to real maternal ECG signals.

## 4 Fetal ECG extraction through phase space reconstruction

We will concentrate here on a technique of extracting a FECCG by use of nonlinear projection. This method was originally proposed in [19] and was later adapted to the general ECG case [39]. The basic idea of this method is the assumption that the fetal component of an ECG recording of a pregnant woman is a contamination (*noise*) of the maternal ECG [36]. The problem of FECCG extraction becomes in this way a problem of noise reduction.

It should be noted here that, if the fetal cardiac component is to be treated as noise that contaminates the maternal ECG signal, a successful noise reduction is not possible using linear noise reduction techniques, such as Fourier filtering in the time domain [50]. The reason is simply that linear filtering will treat experimental noise and the low amplitude FECCG signal equally. In cases where the signal to be extracted is of the same amplitude as the experimental noise, nonlinear noise reduction techniques should be implemented. Such nonlinear techniques are based on the fact that, unlike experimental noise which is random, the signal to be extracted (the FECCG) follows particular dynamics.

In deterministic dissipative dynamical systems, the end point of the trajectory of the system is frequently confined to an *attractor* [1, 25, 36, 25, 43]. The mathematical technique described in this section makes use of the time series of the FECCG recordings to reconstruct the dynamics of the cardiac system of the pregnant mother [25]. The key of the nonlinear noise reduction method described here lies in the idea that, in the absence of experimental noise, the dynamics of this system evolves on an attractor. By estimating this attractor and projecting onto it, noise is expected to be reduced [36]. It should be noted that, as has been demonstrated in [39], chaotic determinism

is not a necessary condition for this method to be successful. Whenever a multidimensional reconstruction of a signal can be approximated by a low-dimensional surface (an attractor), projections onto this (hyper) surface can improve the signal-to-noise ratio [36]. The human ECG is found to spend most of each cycle close to a low dimensional manifold even though, due to random factors in the human body, the ECG is not strictly periodic (there are random fluctuations as far as the length of each cardiac cycle is concerned). An ECG signal can be therefore approximated by dynamics on a low-dimensional attractor [25].

#### 4.1 Phase space reconstruction

To describe the method, let us assume the human circulatory system is a system of many known and unknown variables. Obviously it is impossible to access simultaneous measurements of a number of  $m$  variables of this system. It is possible, however, to record  $m$  values of a particular variable  $s(t)$  that we have access to. Indeed, at each time interval  $t_n$ , where  $n = 1, \dots, N$  and  $N$  is the total number of sampling intervals during the recording, we have access to a particular value of the recorded ECG,  $s(t_n)$ . Introducing the notation  $s(t_n) \equiv s_n$ , our measurements consist of the time series  $\{s_n\}_{n=1}^N$ , see also [36].

It has been shown that, for systems governed by an attractor, it is possible to reconstruct the dynamics of the full system from the time series of just a single variable (see [33] and *Takens embedding theorem* [44]). The reason is that in such systems one variable carries information about all the others. The method is based on *delay plots*, see [1, 25, 36, 43]: assuming a temporal parameter  $\tau$  (the so called *time delay*), a plot of  $s_n$  versus  $s_{n-1}$  (i.e. a plot of the variable against a delayed version of itself) is able to reveal the characteristic shape of the attractor [1, 43]. Such a plot is called a *delay coordinate plot* and has the very important feature that it is able to reproduce the dynamics that would be observed in the phase space of the full system.

When the full system is a system of not only two but  $m$  variables, an  $m$ -dimensional delay plot can be constructed following the same principle: using information from the  $s_n$  measurements backwards in time we introduce the *delay coordinates*

$$\vec{s}_n = (s_{n-(m-1)}, s_{n-(m-2)}, \dots, s_n)$$

to reconstruct the original phase space in an  $m$ -dimensional plot. This

method is called a *delay reconstruction in  $m$  dimensions* and the number  $m$  of the components of  $\vec{s}_n$  is called the *embedding dimension* [1, 25, 36, 43].

It should be noted here that the value of the temporal parameter  $\tau$  is to be chosen interactively. The choice of the optimal time delay  $\tau$  such that the reconstructed attractor can easily be seen in the delay plot is an important and largely unresolved problem and the success of embedding in practice depends heavily on the specific characteristics of the application. The choice of  $\tau$  is typically an art rather than a science: if  $\tau$  is small compared to the time scales of the system then successive elements of  $\vec{s}_n$  will be strongly correlated. If, on the other hand,  $\tau$  is very large, then successive elements of  $\vec{s}_n$  will be already almost independent [25, 43]. It has been shown that the optimal value of  $\tau$  is typically around  $1/10 - 1/2$  of the mean orbital period around the attractor [43]. Often a value of  $\tau$  around the *correlation time* is used; the correlation time is defined as the time  $\delta t$  over which the correlation function  $\langle x(t)x(t + \delta t) \rangle_t$  decays appreciably.

Regarding the choice of the embedding dimension  $m$ , a number of *ad hoc* methods have been proposed that try to estimate whether the attractor has been fully unfolded in an  $m$ -dimensional phase space. The approach of Kennel and Abarbanel [30] is often used, which examines whether points that are near neighbors in one dimension are also near neighbors in the next higher embedding dimension. According to the method, if this does not happen, then the image has not been fully unfolded. If it happens, then the unfolding is complete and the dimension is established. There are, however, still issues as to what constitutes a near neighbor or a false near neighbor [38].

#### 4.1.1 An example of attractor reconstruction: The Lorenz attractor

The Lorenz model [32] was introduced as a simple model of convection in fluids. The equations that describe the model have the form of the following system:

$$\begin{aligned}\dot{x} &= \sigma(y - x) \\ \dot{y} &= rx - y - xz \\ \dot{z} &= xy - bz\end{aligned}\tag{1}$$

where  $\sigma$ ,  $r$  and  $b$  are parameters that characterize the properties of the fluid, as well as of the thermal and geometric configuration of the experiment [7].

The parameter  $\sigma$  depends on the properties of the fluid (it is in fact the ratio of the viscous to thermal diffusivities): Lorenz took the value to be 10 in his paper for the numerical solution of the system (1). For values of  $b = 8/3$  and  $r = 28$  the solution of the system<sup>1</sup> gives the time series for the  $x$  variable shown in figure 4 and, in the three-dimensional space of  $(x, y, z)$ , the solution of the system leads to an attractor, see figure 5.

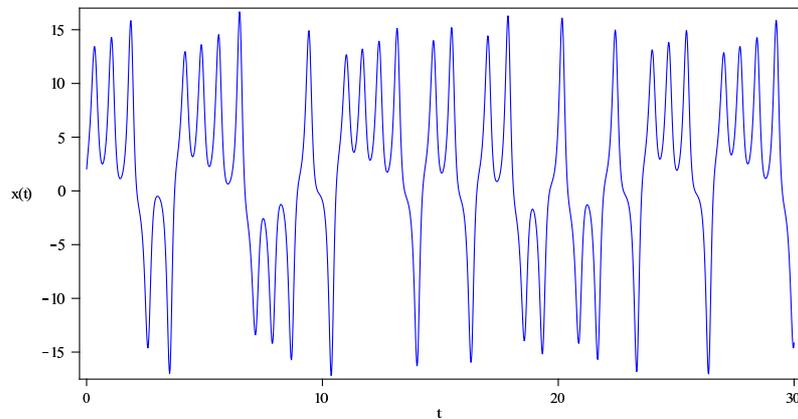


Figure 4: Time series of the  $x$  variable of the solution of the Lorenz system.

The typical trajectory of the Lorenz attractor (figure 5) is a chaotic trajectory, see also [1, 38]. This trajectory orbits one of the two unstable fixed points and eventually escapes to rotate about the other fixed point [7].

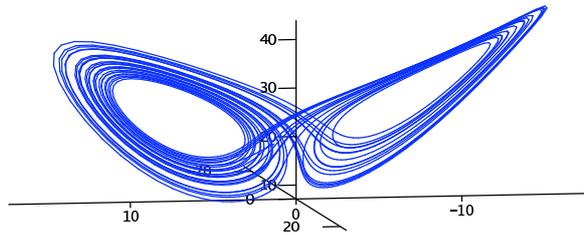


Figure 5: The Lorenz attractor.

According to what we have mentioned before, an attractor of similar

<sup>1</sup>Computations and graphics of this section are done using *Maple*

appearance can be reconstructed from the time series of only one variable, let's say the variable  $x$  [7, 43]. As Lorenz attractor is a three-dimensional attractor, we choose an embedding dimension of  $m = 3$  and construct the delay plot of  $\vec{x}_n = (x_{n-2}, x_{n-1}, x_n)$ , where  $x_n \equiv x(n\tau)$ .

Both figures 5 and 6 have the same *butterfly* appearance [7], i.e. the topological structure of the Lorenz attractor is preserved by the reconstruction.

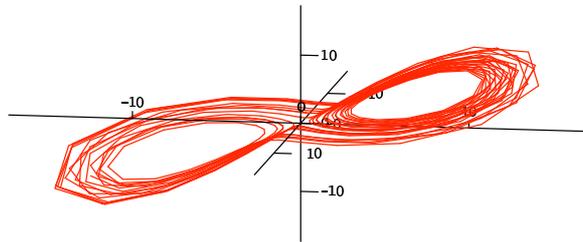


Figure 6: The reconstructed Lorenz attractor taking  $\tau = 0.05$ .

## 4.2 Phase space reconstruction and nonlinear noise reduction

Figure 7 shows two-dimensional delay representations of a simulated electrocardiogram of a pregnant woman represented as a trajectory in the phase space projected on two dimensions. For the graph of figure 7, which is published in [39], the embedding dimension used was  $m = 11$ . As can be observed in figure 7, when a time delay of  $\tau = 0.02s$  is used for the representation, there is a large loop resolving the ventricular QRS cycle, while the smaller features in the center contain the atrial P wave and the T wave, see also [39]. Using a longer time delay such as  $\tau = 0.08s$  the QRS cycle is no longer resolved and there is only a small central loop displaying the T wave.

Having reconstructed the phase space of the full maternal-fetal system from information provided by the maternal ECG, we proceed into extracting the fetal component from the recorded signal. As mentioned before, the fetal ECG signal is considered as nonlinear noise that contaminates the maternal ECG signal. The authors in [36] describe in detail this very effective nonlinear noise reduction algorithm that consists of three steps:

- Step 1: Find a low-dimensional approximation to the attractor described by the trajectory  $\{\vec{s}_n\}$

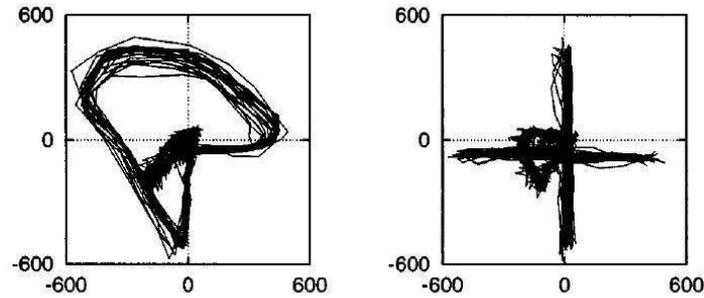


Figure 7: Two-dimensional delay representations of a simulated electrocardiogram of a pregnant woman ( $s_n$  versus  $s_{n-1}$ ). Left:  $\tau = 0.02s$ , right:  $\tau = 0.08s$ . Graph printed in [39], page R4327.

- Step 2: Project each point  $\vec{s}_n$  on the trajectory orthogonally onto the approximation to the attractor to produce a cleaned vector  $\tilde{\vec{s}}_n$
- Step 3: Convert the sequence of cleaned vectors  $\tilde{\vec{s}}_n$  back into the scalar time domain to produce the filtered, noise-free time series  $\tilde{s}_n$ .

For more details on the noise reduction method and its application to FECG extraction see [36, 39].

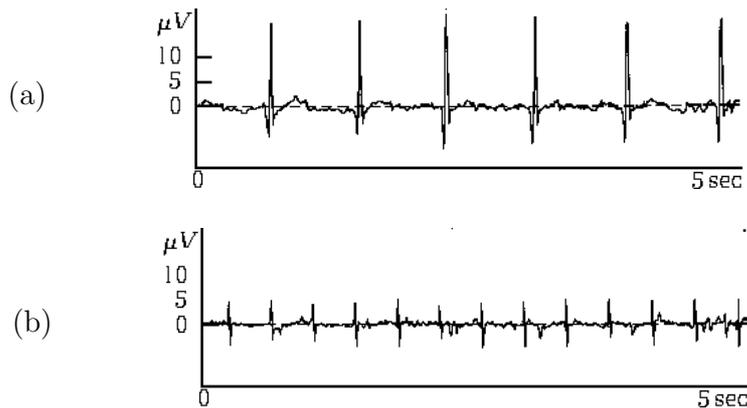


Figure 8: (a): noise-free maternal ECG, (b): FECG, as extracted by the nonlinear projection technique. Figure printed in [36], page 135.

A sample of the results of the method, concerning the extraction of the

fetal component from a maternal ECG is shown in figure 8 (published in [36]). The input signal was the mixed maternal-fetal signal shown in figure 3. Figure 8(a) shows the ("noise"-free) maternal ECG  $\tilde{s}_n$  time series after the implementation of the nonlinear noise reduction method. The extracted FECCG, after reduction of experimental noise, is shown in figure 8(b). The results of the method described in [36], as shown in figure 8 are indeed very impressive.

## 5 Conclusions

Monitoring the heart rate while exercising during pregnancy is essential for both the mother and the fetus. As far as the fetal growth and development is concerned, the effects of maternal physical exercise are found to be strongly dependent on the type, the duration and especially the intensity of exercise. Studies have reached the conclusion that a moderate aerobic exercise during the second and third trimester of pregnancy does not put into risk the healthy development of the fetus [8].



Figure 9: Regulating the heart rate while exercising during pregnancy is of vital importance

In order to avoid any possible problems it is very important to monitor the fetal reaction, as well as the maternal heart rate during physical exercise. Regarding the mother, a simple and accurate way to observe and regulate the heart rate is for example by use of a heart rate monitor [35], see figure 9. The reaction of the fetus can also be easily identified by observation of

the fetal heart rate. For this reason, a number of mathematical tools and techniques, such as the ones described in this review have been developed.

This area is a fascinating test ground for new mathematical tools and techniques, the applications of which have significant implications regarding one of the most important events in the human life span. By the use of such mathematical techniques, the patterns of the fetal response can be revealed and any possible problems can be identified.

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