Original Article

Investigate the Frequency Spectrum of Noise Signals Affecting Synchronous Signals of fMRI and fNIRS in Resting and Moving Wrists

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Functional Near-Infrared Spectroscopy;

Low Frequency Oscillations;

Noise.

Abstract

Purpose: The nerve signals are often contaminated by the non-nerve signals in the same frequency range, i.e. low frequencies in the range of 0.1 Hz. Among the different medical imaging tools, Functional Magnetic Resonance Imaging (fMRI) has been widely used by scientists and scholars due to its high spatial resolution for brain mapping.

Materials and Methods: Also, the use of Functional Near-Infrared Spectroscopy (NFIRS) has continued to rise and regarding its high temporal resolution, it is considered as the complement of FMRI.

Results: However, the effect of non-nerve functions is observed in both methods. Specially, by showing that non-nervous Low Frequency Oscillations (LFOs) 1) are merely non-nervous, because they can be measured by the environmental NIRS; 2) their internal origin is close to the heart; 3) in comparison with the available LF models based on respiration and the merely non-nervous changes in heart, they are unique in their spatial and temporal features, it seems that the systemic signals are moving through the cerebral arteries.

Conclusion: In this paper, LF Oscillations (LFOs) are compared with simultaneous NIRS/FMRI. Also, we discuss the non-neurological effects during simple motions of the wrist in FMRI showing that a significant portion of them, especially in motion state networks, are non-nerve and we measure the sensitivity of NIRS to non-neural LFOs through mapping of nerve and non-nerve LFOs with an extra high spatial and temporal resolution.

1. Introduction

Functional Magnetic Resonance Imaging (fMRI) has been used for brain activity examination in a wide range of studies [1]. When the human brain is affected by a stimulus, blood circulation and oxygen level increases in an especial part of brain according to the task type and fMRI measures the Blood Oxygen Level Dependent (BOLD) area. Also, NIRS is a good technology for human brain examination which has been successful in several applications [2-5]. NIRS is portable [6] and easy to move which has been presented as a useful non-invasive technology for communication between the brain and computer [7-10] this is used for human brain examination in both active and resting states [11-16]. Since fMRI measures the human brain activity indirectly, it is influenced by different factors of blood signals such as oxygenated blood level and blood volume in the brain area under examination, to the extent which nerve activators are responsible.

BOLD signal changes are concentrated through nerve-muscular connection. There is also a large proportion of destructive signals and noise related to magnetic field instability (B0), the effects of which have been observed in human studies and various quality control tools for

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MRI systems [17]. In recent years, a study of neural networks found that noises are not caused by a single neural network and are more biologically or physiologically based due to spontaneous physiological changes, so it can be said that noises cannot be caused by a brain activity [18]. In addition, some researchers have found that the origin of low-frequency signals in the brain is mostly related to arteries and cerebral veins, which means that these signals are not produced by a neural response and are of vascular origin [19, 20]. Some studies also suggest that low frequency signals may be due to circulation or cerebrospinal fluid movement within the cerebral ventricles, or due to deep breathing and oxygen inhalation or heart rate per second [21]. In a study conducted by T. J. Huppert *et al.*, they found that fNIRS in both hemodynamic and peak time models of fMRI modalities had strong correlations as well as fMRI, fNIRS signals of changes in brain activity and increased brain activity. Oxy-hemoglobin has similar sensitivity [22, 23]. In addition, fMRI and FNIRS signals are negatively correlated with the signal dioxide hemoglobin [2].

In this context, using the high fMRI spatial resolution of about 2–3 cm in the three Tesla magnetic fields and the high temporal resolution of the FNIRS, which has a sampling frequency of 10 Hz/s, we decide to combine the two modalities at each strength. Using a combination of fMRI and fNIRS, we can investigate the physiological effects of fMRI, fNIRS on active and resting brain signals, and determine how much they change in different active states.

2. Materials and Methods

Ten healthy right-handed (man) without any movement disorder and/or neurological disorder with an average age of 31(±5.25), aging 27-45 years were selected for this test; all of them signed the informed consent form approved by the Ethics Committee of Tehran University of Medical Sciences. To better pick up the NIRS signal, the motor cortex of the participants' head must be completely shaved, because hair absorbs the light and disturbs the data capturing process. In the previous studies conducted by Yunjie Tong *et al.* for better sampling, the signal was picked up from frontal hairless part of the head. During the test, the participants were asked to lie gently on the scanner bed and open their eyes when capturing the NIRS and fMRI data. During this time, the volunteer was observing a dotted gray plane on which the task of active state of wrist motion was carrying out.

2.1. Designed Test for Volunteers

This study is carried out on healthy people in four steps, including the states of resting, active motion, passive and motion imagination. In the active state, the participants had to do a stage-tracking activity through moving their wrist to the right, left, up, and down while they hold their body steady. In the resting state, they lie fixed on the scanner bed, then the images are captured. For this purpose, in the passive state, the person rests on the bed while the researcher makes the same motion. In the imagined state, the person rests on the couch and, without any movement, thinks only of the movement required of him. Some pictures as shown in Figure 1. were shown to the people through a pair of glasses or a projector MRI compatible; every time one direction was turned on randomly which gave the person the signal to move his hand toward the direction indicated. Right after turning the indicated direction off, the central picture was turned on; at this time the person had to move his hand toward the center from the angle where it was; this made the hand turn back to its natural and neutral state.

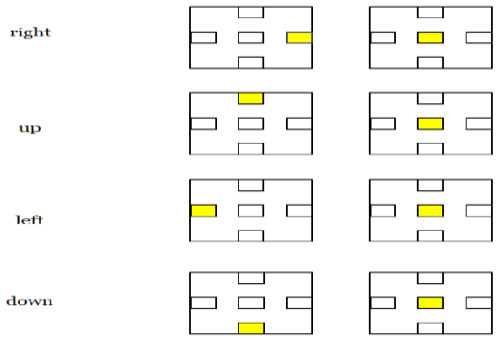

Figure 1. Pattern of movement shown to the volunteer during the experiment

2.2. FMRI Data Acquisition

Before using MRI, initial preparations including changing into a removing the metal objects from body were done. Then, the participant lay within the MRI machine. Four sets of images were taken for every person (Active, Passive, Imaginary, Rest). All MR data were

captured by a Siemens TIM Trio 3 T scanner (National Brain Mapping Lab) and a 20-channel coil array. An anatomical high resolution image set obtained to put slice and amend the functional data which is summarized in Table 1.

Table 1. Parameters of structural images

Scanning Sequence	MP RAGE
Slice Thickness	1 mm
Voxel size	1×1×1 mm^3
Matrix Size	256×256 mm^2
FOV	259 mm
TR	2300 ms
TE	2.97 ms
Flip Angle	9 deg
Number of Slices	176

Second, third and fourth sets include the functional images associated with four states of active, passive, imaginary and resting which are provided by EPI sequence. The image sets of each test state include 248 volumes.

Table 2. Parameters of the functional images in this study

Scanning Sequence	Gradient-Echo EPI
Slice Thickness	3 mm
Voxel size	3×3×3 mm^3
Matrix Size	64×64 mm^2
FOV	210 mm
TR	2000 ms
TE	30 ms
Flip Angle	90 deg
Number of Slices per TR	34
Number of Volumes	248
Multi-Slice Mode	Interleaved

2.3. NIRS Data Acquisition

FMRI and FNIRS data were simultaneously captured in national brain mapping lab with a 48-channel FNIRS machine compatible with MRI, called Oxy Mon fNIRS manufactured by Artinis Co. In this project, totally 20 channels (16 optods as receiver and 16 optods as transmitter) placed on the motor cortex as shown in Figure 2. The protocol was approved by surveillance board of national brain mapping lab (in previous studies, a total of 3 channels were used for data capturing) [24]. The probe is a fiber optic transmitter that each light emitting fiber is made up of two laser diode layers emitting 690 and 830 nm wavelengths. The laser diodes and light detectors (photomultiplier tube Hamamatsu Photonics R928) placed in MRI control room for tissue near infrared imaging (Imagent ،ISS ،Inc. ،Champaign ، Illinois). The sampling rate of NIRS data was 10 Hz. Then the participant was asked to lie on the bed and do the task steps as he was trained previously.

2.4. NIRS Data Acquisition

At the same time that fMRI and fNIRS signals are picked up, a pulse oximeter is connected to the participant's fingertip then the blood circulation signals are picked up and recorded.

2.5. Respiratory Signal Picking up

At the same time that fMRI and fNIRS signals are picked up, the belt available on the MRI machine is fastened on the participant’s chest, then the respiratory signals and respiratory motions are picked up and recorded for processing.

2.6. Functional Magnetic Resonance Image Data Analysis

Both NIRS and fMRI data of each volunteer were analyzed by FEAT that is a part of FSL analysis package FMRIB Expert Analysis Tool, v5.98, http://www.fmrib.ox.ac.uk/fsl, (Oxford University, UK). The fMRI preprocessing steps include: Motion correction, slice time correction, spatial smoothing (filter FWHM = 5mm) and high pass filtering in time domain (cutoff frequency = 0.02 Hz to eliminate very slow noise of the tools).

2.7. NIRS Data Analysis

In this project, as shown in Figure 2, totally 20 channels placed on motor cortex of the head to capture the NIRS data. After analyzing the fMRI data and obtaining the active area based on the MNI location of each channel, the channels that were in the active area were determined. Then the data of these channels were used to process and analyze the FNIRS time series.

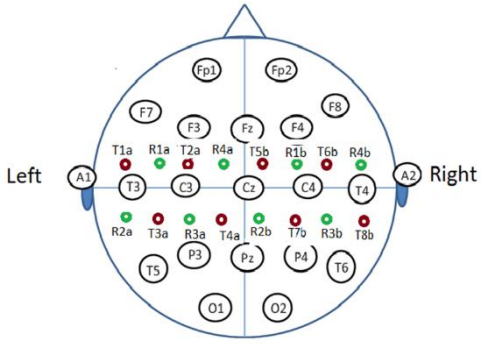

Figure 2. Location of optods and channels designed for signal picking up

2.8. Fourier Transform and Destructive Signals Investigation

To better understand the frequency band of the destructive and noise signals, we applied a Fourier transform to the signals in Active, passive, motion imagination and resting states. Also, the Fourier transform was applied to the environmental signals measured by pulse oximeter and the respiratory signal measured by the respiratory belt.

3. Results

Nerve activity of blood in the active area of brain is more than what is needed for response to that activity. This effect is called hemodynamic response function. The hemodynamic response is slow and starts growing within 2-3s and reaches to the maximum within 5-6s. After 15s, it starts decreasing (falling). The indirect nerve response is measured in the low frequency range; even in absence of a task, the brain activity in the fix muscles makes the signal has constant oscillations within the low frequency range. These low frequency oscillations (LFOs) are often representative of the related nerve activity in the different parts of the brain. However, whereas most nerve activities are observed in the low-frequency range, considerable pieces of evidence show that at least some part of LFOs observed in the brain imaging studies are non-nervous. As mentioned above, physiological noises make disruption in the nerve signals and destroy the data. In this study, our purpose is to find the frequency of nerve signals as well as the noise and destructive signals in the resting, active, passive and motion imaginary states that have been presented as the nerve signal and the pulse oximeter and respiratory signals as destructive and noise signals for better understanding of the frequency band of each mode. The brain blood has a high oxygen saturation which varies from 100 % in arterial blood to 60 % in venous blood and its high ratio is the ratio of [HbO] to Hb. The studies show that the magnitude of signal Δ [HBO] (and signal to noise ratio (SNR)) is almost 3-4 times the magnitude of Δ [HBO] [24]. Therefore, in this study we considered Δ [HBO] as a reference signal. According to the Fourier transform applied to the signals, the following results were obtained. Figure 3. shows the frequency spectrum of the Δ [HBO] measured by NIRS on the selected path in the channel selection step, the environmental pulse measured by the pulse oximeter, and the respiratory belt wavelengths of the volunteer 9 in the different states (volunteer 9 was selected owing to its high SNR).

3.1. Results of Frequency Spectrum Analysis of the Signals Obtained in Resting Mode of Simple Motion of the Wrist Data

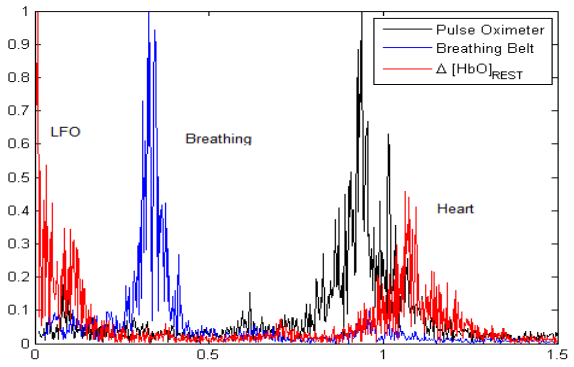

Figure 3. Plot of the frequency spectrum for oxy-hemoglobin, respiratory belt, and pulse oximeter signals in the resting mode

Figure 3. shows the frequency spectrum of the physiological signals (respiratory belt and pulse oximeter) in the resting mode. The horizontal axis represents the frequency band in Hz and the vertical axis represents the magnitude of different signals. The red, blue and black plots represent the changes of oxy-hemoglobin density, respiratory belt frequency spectrum and the pulse oximeter, respectively. The center frequency of each modality has been shown in Table 3.

Table 3. Frequency spectrum center of different signals in resting state

Volunteer No.	Age (years)	Gender	Task Duration	NIRS Center	Respiratory Belt Center (HZ)	Pulse Oximeter Center (HZ)
Volunteer 1	32	Male	8:42	0.9	0.4	0.9
Volunteer 2	32	Male	8:42	0.9	0.3	0.9
Volunteer 3	27	Male	8:42	0.9	0.4	0.9
Volunteer 4	29	Male	8:42	1	0.4	1
Volunteer 5	31	Male	8:42	1.2	0.2	1.1
Volunteer 6	28	Male	8:42	1	0.3	1
Volunteer 7	45	Male	8:42	1.2	0.2	1.2
Volunteer 8	27	Male	8:42	1	0.4	1
Volunteer 9	30	Male	8:42	0.9	0.2	0.9
Volunteer 10	29	Male	8:42	1	0.3	1.2

3.2. Results of Frequency Spectrum Analysis in the Active Mode of Simple Motion of the Wrist

Figure. 5 shows the frequency spectrum of the physiological signals (respiratory belt and pulse oximeter) in the motion imagination mode. The horizontal axis represents the frequency band in Hz and the vertical axis represents the magnitude of different signals. The red, blue and black plots represent the changes of oxy-hemoglobin density, respiratory belt frequency spectrum and the pulse oximeter, respectively. The center frequency of each modality has been shown in Table 5.

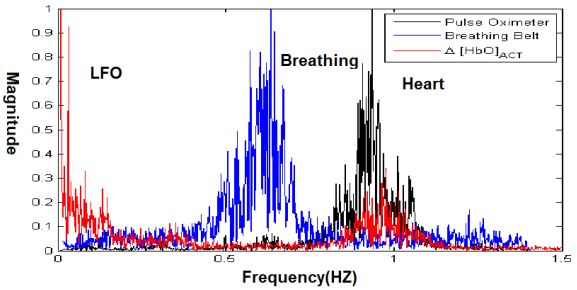

Figure 4. Plot of the frequency spectrum for oxy-hemoglobin, respiratory belt, and pulse oximeter signal in active mode

Table 4. Frequency spectrum center of different signals in the active mode

Volunteer No.	Age (years)	Gender	Task Duration	NIRS Center	Respiratory Belt Center (HZ)	Pulse Oximeter Center (HZ)
Volunteer 1	32	Male	8:42	1	0.5	1
Volunteer 2	32	Male	8:42	0.8	0.3	0.8
Volunteer 3	27	Male	8:42	0.9	0.3	0.9
Volunteer 4	29	Male	8:42	1	0.6	1
Volunteer 5	31	Male	8:42	1	0.4	1
Volunteer 6	28	Male	8:42	1	0.4	1
Volunteer 7	45	Male	8:42	0.9	0.3	0.9
Volunteer 8	27	Male	8:42	1	0.5	1
Volunteer 9	30	Male	8:42	0.9	0.3	0.8
Volunteer 10	29	Male	8:42	1	0.4	0.9

3.3. Results of the Frequency Spectrum Analysis in the Motion Imagination Mode of Simple Motion of the Wrist

Figure. 5 shows the frequency spectrum of the physiological signals (respiratory belt and pulse oximeter) in the motion imagination mode. The horizontal axis represents the frequency band in Hz and the vertical axis represents the magnitude of different signals. The red, blue and black plots represent the changes of oxy-hemoglobin density, respiratory belt frequency spectrum and the pulse oximeter, respectively.

The center frequency of each modality has been shown in Table 5.

Table 5. Frequency spectrum center of different signals in the motion imagination mode

Volunteer No.	Age (years)	Gender	Task Duration	NIRS Center(HZ)	Respiratory Belt Center(HZ)	Pulse Oximeter Center (HZ)
Volunteer 1	32	Male	8:42	1	0.4	1
Volunteer 2	32	Male	8:42	0.8	0.2	0.8
Volunteer 3	27	Male	8:42	0.9	0.3	0.9
Volunteer 4	29	Male	8:42	0.9	0.7	0.9
Volunteer 5	31	Male	8:42	1	0.2	1
Volunteer 6	28	Male	8:42	1	0.3	1
Volunteer 7	45	Male	8:42	1	0.2	1
Volunteer 8	27	Male	8:42	1.1	0.4	1.1
Volunteer 9	30	Male	8:42	1	0.3	0.9
Volunteer 10	29	Male	8:42	0.9	0.2	0.8

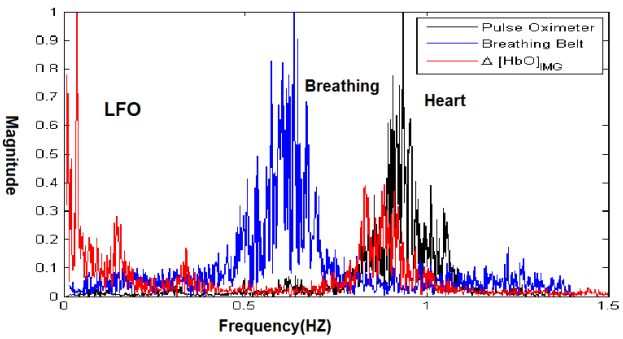

Figure 5. Plot of the frequency spectrum for oxy-hemoglobin, respiratory belt, and pulse oximeter signals in the imagination mode

3.4. Results of the Frequency Spectrum Analysis in the Passive Mode of Simple Motion of the Wrist

Figure 6. shows the frequency spectrum of the physiological signals (respiratory belt and pulse oximeter) in the passive mode. The horizontal axis represents the frequency band in Hz and the vertical axis represents the magnitude of different signals. The red, blue and black plots represent the changes of oxy-hemoglobin density, respiratory belt frequency spectrum and the pulse oximeter, respectively. The center frequency of each modality has been shown in Table 6.

Table 6. Frequency spectrum center of different signals in the motion passive mode

Volunteer No.	Age (years)	Gender	Task Duration	NIRS Center	Respiratory Belt Center (HZ)	Pulse Oximeter Center (HZ)
Volunteer 1	32	Male	8:42	0.9	0.4	0.9
Volunteer 2	32	Male	8:42	0.8	0.3	0.8
Volunteer 3	27	Male	8:42	1	0.3	1
Volunteer 4	29	Male	8:42	0.9	0.4	0.9
Volunteer 5	31	Male	8:42	0.9	0.3	0.9
Volunteer 6	28	Male	8:42	1	0.4	1
Volunteer 7	45	Male	8:42	1.2	0.2	1.2
Volunteer 8	27	Male	8:42	1	0.4	1
Volunteer 9	30	Male	8:42	0.8	0.2	0.9
Volunteer 10	29	Male	8:42	1.2	0.3	1

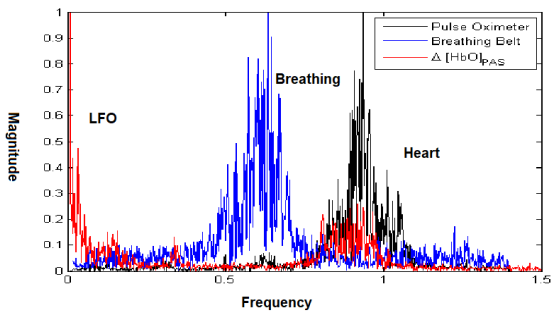

Figure 6. Plot of the frequency spectrum for oxy-hemoglobin, respiratory belt, and pulse oximeter in the passive mode

4. Discussion

In this section, we analyze and discuss the results mentioned in the previous sections more. In brain, the nerve activities change with different activities such as walking, reading, and imagination. There are different patterns of brain activity for sensory perception including vision and touch. Even in the resting mode, there are special patterns which indicate that some particular networks in the brain work together. The functional imaging techniques measure this activity to understand how a healthy brain works or how it is disrupted in the pathological cases. The nerve activity of blood in active area of the brain is more than what is needed for response to that activity. This effect is called hemodynamic response function. The hemodynamic response is slow and starts growing within 2-3s and reaches the maximum within 5-6s. After 15s, it starts decreasing (falling). The indirect nerve response is measured in the low frequency range; even in absence of a task, the brain activity in the fix muscles makes the signal has constant oscillations within the low frequency range. These low frequency oscillations (LFOs) are often representative of the related nerve activity in the different parts of the brain. However, whereas most nerve activities are observed in this frequency range, considerable pieces of evidence show that at least some part of LFOs observed in the brain imaging studies are non-nervous. As mentioned above, the physiologic noises make disruption in the nerve signals and destroy the data. In this study, our purpose is to find the frequency of nerve signals as well as the noise and destructive signals in the resting, active, passive and motion imaginary states that have been presented as the nerve signal and the pulse oximeter and respiratory signals as destructive and noise signals for better understanding of the frequency band of each mode. The brain blood has a high oxygen saturation which varies from 100 % in arterial blood to 60 % in venous blood and its high ratio is the ratio of to [HbO]. The studies show that the magnitude of the signal Δ [HBO] (and signal to noise ratio (SNR)) is almost 3-4 times to the magnitude of Δ [HbO] [24]. Therefore, in this study we considered Δ [HBO] as the reference signal.

To better understand the LFO components of NIRS signal, we applied a Fourier transform to the environmental signals including respiratory belt, pulse oximeter as well as the NIRS signal in all active, passive and motion imagination states; some of the results are as follows:

1) The average frequency of ECG signal picked up by the oximeter is nearly 1Hz for all participants, which is similar to the previous studies. Therefore, the cardiac frequency is a prominent component of the NIRS signal in all cases which causes disruptions in the signals of functional and resting modes. So, a proper filter is needed to be applied when removing the noise of ECG signal. The above findings were in accordance with the study of Y. Tong *et al.* which was carried out in the resting mode. The difference is that Tong *et al.* picked up the signal from the frontal lobe because it was bald. But in this study, for simultaneous study of the active and resting modes of the brain, we captured the data from motor cortex of the bald persons. Therefore, data capturing area doesn't make any significant difference in frequency band of the noise signals.

2) The average respiratory frequency derived from the respiratory belt has center frequency of 0.3 Hz which is in accordance with the study of Greve *et al.*[25] Direct effect of the respiratory waveform on the NIRS data (for example in the fundamental respiratory frequency) is relatively small and variable. It should be mentioned that the trivial changes in breathing or breath depth may affect the data out of this group (as presented by Birn *et al.*) [26]. These effects are a part of LFO signal and the effects sensitive to the gaps between breaths that influence the fMRI time series duo to its low temporal resolution and make disruption in time series and the brain map. But, as observed, LFOs have little effect on NIRS time series duo to its high temporal resolution. Duo to the high

correlation between these two modalities, NIRS data can be used as a regressor to improve the fMRI brain patterns.

3) LFOs were observed in NIRS data in the marginal frequencies less than 0.1 Hz but not in pulse oximeter and respiratory belt which may be resulted from high pass filtering in the physiological recording system. This project analyzes the right-hand activity in the primary motor cortex of the left brain lobe, but this may be implemented for no dominant hand through designing a motion test in the left hand of the left-handed people to find the similarities and differences.

This test can be simultaneously carried out by other modalities such as EEG, then its results can be compared with results of our study to find the similarities and differences.

5. Conclusion

According to the descriptions and studies done in the past, it can be stated that the main factors affecting the brain signals include heart rate, respiratory rate, chest wall motions, as well as spontaneous motions of the vessel wall, which are referred to as low frequency signals. It can also be stated that, depending on the frequency spectrum of the signals, the frequency range of the destructive agents and the noise does not change in the active-passive state and the motion assumption, so it can be suggested that in the BOLD fMRI analyzes in the active-passive state and the motion assumption signals use the filters required above.

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