A Quasi-Local Method for Instantaneous Frequency Estimation With Application to Structural Magnetic Resonance Images

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Abstract— **Spatially-varying signal content can be effectively modeled using amplitude modulation-frequency modulation (AM-FM) representations. The AM-FM representation allow us to extract instantaneous amplitude (IA) and instantaneous frequency (IF) components that can be used to measure non-stationary content in biomedical images and videos. This paper introduces a new method for estimating the IA and the IF based on a quasi-local method (QLM).**

We provide an extensive comparison of AM-FM demodulation approaches based on QLM and a quasi-eigenfunction approximation method using three different filter-banks: (i) a separable, equiripple design, (ii) a Gabor filter bank, and (iii) a directional filter bank approach based on the Contourlet transform. The results document that the use of the new QLM method with an equiripple filter bank design gave the best IF magnitude estimates for a synthetic image.

The new QLM method is then applied to a multi-site schizophrenia dataset (N=307). The dataset included structure magnetic resonance images from healthy controls and patients diagnosed with schizophrenia. The IF magnitude is shown to be less sensitive to variations across sites as opposed to the standard use of SMRI images that suffered from significant dependency on the scanner configurations on different collection sites. Furthermore, the regions of interest identified through the use of the IF magnitude are in agreement with previous studies.

I. Introduction

Biomedical images are often dominated by strong non-stationary behavior that can be described using Multidimensional Amplitude Modulation-Frequency Modulation (AM-FM) models [1], [2]. The development of AM-FM models and applications have been documented in previous research reported in [3], [4], [5], [6], [7].

In general, the AM-FM representation of an image $I(\mathbf{x})$ is expressed as:

$$I(\mathbf{x}) = \sum_{n=1}^{M} a_n(\mathbf{x}) \cos(\varphi_{\mathbf{n}}(\mathbf{x})) \quad (1)$$

where $\mathbf{x} = (x_1, x_2, \dots)$ denotes the pixel coordinates, $M \in \mathbb{N}$ indicates the number of components, $a_n > 0$ denotes the n-th instantaneous amplitude (IA) function, and φ_n denotes the n-th instantaneous phase (IP) function. In eq. (1), the image is decomposed into M components given by $a_n(\mathbf{x}) \cos(\varphi_n(\mathbf{x}))$, where $\cos(\varphi_n(\mathbf{x}))$ are the FM components from which the instantaneous frequency (IF) and IP are estimated. Here, the IF is defined as the gradient of the IP: $\nabla\varphi(\mathbf{x})$. The use of an AM-FM model for describing non-stationary content requires the estimation of the IA, IP, and IF components from each input image.

Estimation of the AM-FM components can be performed using a quasi-local method (QLM) or an adaptive quasi-eigenfunction approximation (QEA) method as given in [8]. For both methods, AM-FM components are estimated over a set of band-pass filters (filter bank). In this paper, we will investigate the use of different filter bank and AM-FM component estimation methods configurations.

Overall, the current paper provides the following:

- **IF estimation based on QLM that does not impose frequency magnitude bounds:** The current paper extends the research presented in [8] by not requiring the use of frequency magnitude bounds for IF estimation. By removing this restriction, the new approach allows the use of directional filter banks prior to AM-FM component estimation.
- **Comparisons of multiple AM-FM method configurations:** We test 6 possible configurations including the proposed demodulation method, QEA and three filter-banks designs. We investigate estimation errors in the presence of additive Gaussian noise and then identify the best algorithm.
- **AM-FM decomposition of structural magnetic resonance images (SMRI):** To the best of our knowledge, this paper presents the first application of AM-FM models to represent a SMRI dataset used for investigating mental illness.
- **Application to a Schizophrenia case-control dataset:** We apply the best AM-FM decomposition configuration to a Schizophrenia study with 307 subjects and validate reported regions with the literature.

The rest of this paper is organized as follows: in section II, we present the AM-FM decomposition, the simulation framework, and the experimental Schizophrenia case-control dataset; in section III, we present the results of the simulation and application and discuss them; and in section IV, we present our conclusions.

II. Materials and Methods

In this section we present the new the quasi-local method (QLM) and the original quasi-eigen approximation (QEA) [9], used to decompose signals into its AM-FM components. We also describe the methodology followed to compare the two demodulation methods in combination with 3 filter

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bank designs: Gabor, equirriple, and directional. Finally, we describe the dataset in which the best AM-FM configuration was applied.

A. Generalized quasi-local method

The QLM constrains the decomposition to signals with frequencies lying on the lower half of the Nyquist limit. Even though an extension of QLM, proposed in [8], allows to compute the signal with frequency content on the higher half, the signal's frequency content has to be on either half of the spectrum. This limits the variety of filter-bank designs that can be used in an AM-FM decomposition framework, especially affecting directional designs.

We overcome this issue by proposing a new Quasi-local method that supports signals with an unknown frequency content. Since this approach is separable, we develop the one-dimensional algorithm that is then applied to each dimension.

The QLM proposes the estimation of $\omega(x) \in [0, \frac{\pi}{2}]$ as in

$$\omega(\boldsymbol{x}) = \cos^{-1}\left(\frac{R(\boldsymbol{x}) + \sqrt{R^2(\boldsymbol{x}) + 8}}{4}\right) \tag{2}$$

where

$$R(\boldsymbol{x}) = \frac{2\breve{g}_{(1,1)}(\boldsymbol{x})}{\breve{g}_{(1,0)}(\boldsymbol{x}) + \breve{g}_{(0,1)}(\boldsymbol{x})},$$

and

$$g_{(\boldsymbol{\epsilon}_1,\boldsymbol{\epsilon}_2)} = I(\boldsymbol{x}+\boldsymbol{\epsilon}_1)I(\boldsymbol{x}-\boldsymbol{\epsilon}_2),\ \boldsymbol{\epsilon}_1, \boldsymbol{\epsilon}_2 \geq 0$$

On the other hand, the QLM extension proposed in [8] estimates $\omega(x) \in [\frac{\pi}{2}, \pi]$ as in

$$\omega(\boldsymbol{x}) = \pi - \cos^{-1}\left(\theta(-R)\right), \tag{3}$$

where, $\theta(R)$ denotes the argument of $\cos^{-1}(\cdot)$ in eq. (2).

Our extension propose the estimation of $\omega(x) \in [0, \pi]$ exploiting the fact that $R \in (-\infty, 1], \forall\omega \in [0, \frac{\pi}{2}]$, and $R \in [-1, +\infty), \forall\omega \in [\frac{\pi}{2}, \pi]$.

To extend the method for arbitrary frequencies, we examine the value of R to determine the IF component estimates. Since $\theta(R)$ is a monotonically increasing function, we have that $R \in (-\infty, -1]$ implies that $\omega \in [0, \frac{\pi}{3}]$. Similarly for $\theta(-R)$, for $R \in (1, -\infty]$, we will have that $\omega \in [\frac{2\pi}{3}, \pi]$. Thus, based on R, we estimate each IF component using eq (2) when $R \in (-\infty, -1]$ and (3) when $R \in (1, -\infty]$. Then, we still have the remaining case when $R \in [-1, 1]$. In this case, we generate two estimates by: (i) using a low-pass filter with a passband of $[0, \frac{\pi}{2}]$ and then use eq. (2) to generate the low-frequency estimate, and (ii) using a high-pass filter with support on $[\frac{\pi}{2}, \pi]$ and then use eq. (3) to generate the high-frequency estimate. Between the two estimates, we then select the estimate that gave the larger IA estimate.

B. Simulation framework

We test the proposed QLM based method and QEA with three filter-bank designs. The first filter-bank is designed as a separable equirriple with 3 scales, passband ripple set to 0.017 dB, stopband attenuation set to 30 dB, and transition bands set to $\frac{\pi}{10}$. The second filter-bank follows a Gabor transform design set to 3 scales and 8 directions with increasing spreads for higher frequencies. The last filter-bank follows a multiresolution directional design [10] with 3 scales and 8 directions. We chose the best configuration based on the IF estimation error tested on a synthetic image.

We generate the synthetic image using

$$I(\mathbf{x}) = \cos\left(\frac{a}{3}x_1^3 + \frac{a}{3}x_2^3 + cx_1 + cx_2\right),\ \forall x_1, x_2 \in [-1, 1]. \tag{4}$$

Here, we have that $\varphi(\boldsymbol{x}) = (\frac{a}{3}x_1^3 + \frac{a}{3}x_2^3 + cx_1 + cx_2)$, and $\nabla\varphi(\boldsymbol{x}) = \omega(\boldsymbol{x}) = (ax_1^2 + c, ax_2^2 + c)$. We set $c = -\frac{\pi}{8}$, and $a = \pi - c$ to achieve a maximum IF of π at the borders of the image. We use Gaussian additive noise to perturbate the synthetic image and increase the standard deviation to emulate higher levels of noise. The synthetic image is set to 512×512 pixels. We then conduct an AM-FM decomposition of the synthetic image using all the mentioned configurations and measure the IF estimation MSE. We then investigate the error for $0.01\pi \leq |\omega| \leq 0.99\pi$. We also ignore boundary artifacts by only measuring errors that are at-least 5 pixels away from the boundary of the image, i.e. we do not consider the error in the upper, lower, left, and right edges of the image.

C. AM-FM decomposition of sMRI

Structural magnetic resonance imaging (sMRI) is a popular brain imaging technique that can be used to measure gray matter concentration (GMC). The process of obtaining sMRI images is non-invasive and results in a three-dimensional picture of the subject's GMC structure [11].

Several studies make use of large sMRI datasets to provide evidence of GMC variations generated by neuro-degenerative diseases such as Schizophrenia, Alzheimer's disease, Bipolar disorder, among others. However, the subtle differences and extensive variety of reported regions suggests that the detection of such regions still remains a challenge.

Classic approaches for the identification of regions of interest on GMC rely on the use of statistical parameter mapping. This technique consists on reporting the statistical significance of a voxel tested against a disease of interest. However, this procedure does not exploit spatial properties of GMC and test each voxel independently. A more recent approach, [12], proposed the use of a scale invariant feature transform (SIFT) that extract high-level features to characterize sMRI and report regions of interest. This approach does take into account spatial properties of sMRI but does not provide a representation at a voxel level on the image, possibly missing important brain features. On the other hand, a complete representation of the spatial characteristics of sMRI such as an AM-FM decomposition will thoroughly exploit this intrinsic property of the data.

Specifically, we propose the use of the IF functions to describe sMRI texture. The brain is formed of peaks and valleys, called gyri and sulci, which exhibit a wavy pattern across the brain. The three-dimensional IF captures this pattern in direction (orthogonal to edges) and magnitude (rate of intensity variation). Therefore, the IF magnitude will be

TABLE I: Demographics of MCIC and COBRE studies.

Site	Control/Case	Male/Female	Age±sd
New Mexico	61/53	89/25	36±12.8
Minnesota	19/30	34/15	32.2±10.6
Massachusetts	24/28	32/20	38.7±9.3
Iowa	60/32	59/33	31.3±10
Total	164/143	214/93	34.46±11.4

able to characterize the concavities and provide a quantitative measure on the geometry of the brain structure.

D. Experimental Dataset

This study combined data from two studies: the Mind Clinical Imaging Consortium (MCIC), a multi-center collaborative study (University of New Mexico - Mind Research Network, Massachusetts General Hospital, University of Minnesota, University of Iowa) of schizophrenia patients; and the Center for Biomedical Research Excellence (COBRE), a multidisciplinary study on brain function and mental illness hosted at the University of New Mexico-Mind Research Network.

The MCIC patient group comprised subjects that met DSM-IV-TR criteria for schizophrenia, schizophreniform disorder, or schizoaffective disorder. The diagnoses were based on DSM-IV criteria using the Structural Clinical Interview for DSM Disorders (SCID). Similarly, the COBRE patient group comprised schizophrenia patients screened using DSM-IV criteria. The healthy control group included participants with no history of neurological or psychological disorder screened by SCID.

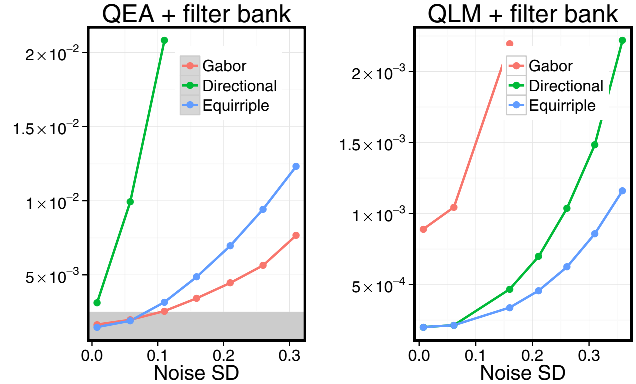
The MCIC controls were screened using the SCID, and subjects were excluded who were diagnosed with substance abuse/dependence, medical, psychiatric, or neurological illnesses. Healthy controls were not excluded if they had been medicated with antidepressants, antianxiety, or sleep deprivation medications, so long as these medications had not been taken for at least 6 months prior to the scan and for not more than 2 months of continuous use at any time.

We extracted 307 subjects for the purpose of this study where 157 were schizophrenia patients and 177 healthy controls. Demographic information and number of subjects per site is listed in Table I. Details on sMRI adquisition can be obtained in [13].

The length of each dimension in our sMRI dataset is 91, thus we adjust the design of the equirriple filter-bank to 2 scales, maximum amplitude ripple of 0.02 in the pass band, 0.2 maximum amplitude ripple in the rejection band and a 10% frequency spacing for the transitions. This results in 17 coefficients per filter which exhibits a reasonable size compared to the dimension length of our dataset.

III. Results and Discussion

The simulation results (see Fig. 1) indicate that the best configuration for IF estimation, under the presence of additive Gaussian noise, is the QLM based method with an



(a) (b)

Fig. 1: Normalized error comparisons for different filter-banks. (a) Filter bank comparison using QEA, and (b) QLM. The dots denote the mean error after 50 repetitions at the given noise level. The shaded area in the left plot denotes the vertical range plotted in the right plot.

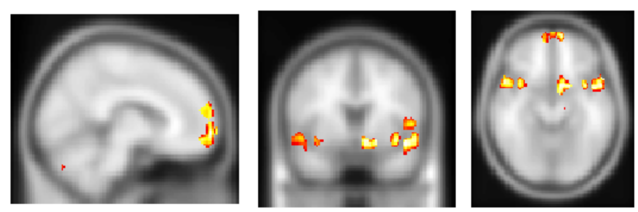


Fig. 2: Sagital, coronal and axial view of voxels that are significantly different (passing FDR correction) among schizophrenia patients and healthy controls

equirriple filter-bank design. In fact, all three configurations using QLM exhibited a better performance than QEA based estimations.

Regarding the filter-bank design, a flat pass-band filter such as the separable equirripple, provided the most accurate results compared to a Gabor-like design because it avoids the necessity of an amplitude correction which induces numerical instability. Also, the simple implementation of the separable filter-bank compared to the complex process of the multi-resolution directional filterbank favored the election of an equirriple design.

After identifying the best AM-FM decomposition configuration, we decomposed the experimental dataset described in sec. II-D. The estimated IF magnitude of SMRI for each subject was in the interval $[0, 0.17\pi]$. IF captured patterns with instantaneous wavelength of 1.25 cm and higher. This is not surprising since a smoothing pre-processing step that used a full-width half maximum (FWHM) Gaussian kernel of 1 cm was applied as in [13], so any texture smaller than 1 cm is significantly attenuated.

We then test the robustness of IF to multi-site effects (4 collection sites, see Table I) conducting an analysis of variance (ANOVA) test to the healthy control group in the study. The test indicates that using GMC 170,806 voxels (91.6% of intracraneal voxels) were significantly different among sites after multiple comparison correction (FDR$<$ 0.01) while just 15,539 voxels (8.3%) exhibited such difference for IF magnitude. The considerable reduction of affected voxels provides evidence that a texture measure such as IF magnitude is less affected by intensity variations due to scanner variability.

Since the effect of the collection site on IF magnitude is small, we conducted a voxel-wise two sample t-test using IF magnitude to identify brain regions significantly different between schizophrenia patients and healthy controls. According to the Taliarach coordinate system, the most significantly different regions overlap the superior temporal gyrus, parahippocampal gyrus and medial frontal gyrus (see Fig. 2). None of these regions overlapped the few scattered voxels affected by collection site or gender.

Several reports on the literature validate this results for schizophrenia [14] suggesting that the instantaneous wavelength can provide meaningful result. In our study, the most significantly different voxel showed schizophrenia patients with mean instantaneous wavelength of 8.3 cm and 7.1 cm for healthy controls, implying the formation of slower intensity variations in schizophrenia patients. The IF magnitude on SMRI measured patterns of sulci and gyri formation on the two groups of subjects, revealing abnormalities that affect schizophrenia patients.

A SMRI study focused on the GMC of gyri and sulci in schizophrenia relatives and controls, [15], suggested cingulate and superior temporal sulcal thickness abnormalities than may be associated with a genetic liability to schizophrenia. Our study suggests a schizophrenia abnormality on the superior temporal gyrus which may be affected by superior temporal sulcal malformation reported in [15] for schizophrenia patients.

IV. Conclusion

In this paper, we presented a new AM-FM demodulation method and demonstrated its application to SMRI. The proposed approach showed that the IF magnitude was associated with previously investigated disease regions that were not affected by different site effects. In fact, the proposed approach showed significantly less site dependency than the standard use of GMC. This information can be used to complement SMRI studies on the effect of neuro-degenerative diseases to sulci and gyri formations.

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