Theoretical Performance and Sampling Limits in Steady-State Magnetic Resonance Elastography

Joshua Trzasko[1], Kevin Glaser[1], Arvin Arani[1], Armando Manduca[1], David Lake[1], Phillip Rossman[1], Shivaram Poigai Arunachalam[1], Kiaran McGee[1], Richard Ehman[1], and Philip Araoz[1]

[1]*Mayo Clinic, Rochester, MN, United States*

Target Audience: Clinicians and scientists interested in magnetic resonance elastography (MRE) or image reconstruction theory.

Purpose: MRE is an increasingly popular magnetic resonance imaging (MRI) application where mechanically induced motion is estimated from a time-encoded series of phase-contrast images [1] and used to generate quantitative spatial maps of tissue stiffness [2]. Like most dynamic/parametric applications, MRE has some flexibility regarding acquisition parameter assignment. For motion-encoding gradients (MEG) – a key element of MRE – the user controls the number of phase offsets, motion-encoding directions ($\boldsymbol{D} \in [\mathbf{1}, \mathbf{3}]$), and excitations (NEX), MEG polarities, use of reduced [3] or fractional encoding [4], and execution of mono- or multi-directional encoding (e.g., Tetrahedral [5], SLIM [6]). These degrees of freedom have bred variability in how MRE data is acquired within and across research groups, and sparked debate over which protocols are "better" than others. Objective settlement of such debates requires comparison of concrete performance measures. Effort towards this direction has been made (e.g., [7,8]); however, all optimization and valuation platforms developed so far start with the motion-induced phase signal. This is problematic for two reasons: 1) the signal dependence and spatial non-uniformity of phase noise [9] compromises the accuracy of statistical characterization; and 2) ignoring spin density and static phase information results in an underestimation of MRE signal processing complexity. In this work, starting from the raw, complex MR image series, we derive the Cramer-Rao Lower Bound (CRLB) for the harmonic signal, which completely describes mechanically induced motion in single-frequency, steady-state MRE. The CRLB defines the minimum achievable covariance of any (unbiased) harmonic estimator and, consequently, the performance limit of an experimental setup. We then identify the minimum number of data samples needed for complex harmonic estimation to be well-posed. Finally, we experimentally validate the harmonic CRLB across a range of acquisition settings to demonstrate its predictive accuracy.

Methods: The signal associated with a single voxel within a steady-state MRE image series can be modeled as $\boldsymbol{f}(n) = \boldsymbol{m}\exp\{\mathrm{j}\boldsymbol{Re}\{\boldsymbol{\delta}_n^T\boldsymbol{G\eta}\}\} + \boldsymbol{z}(n)$, where $n \in [\mathbf{1}, \boldsymbol{N}]$ is the time index, $\boldsymbol{m}$ is the (complex-valued) non-motion-encoded transverse magnetization, $\boldsymbol{\delta}_n$ is Kronecker's delta, $\boldsymbol{z}$ is zero-mean proper complex Gaussian noise with channel variance $\boldsymbol{\sigma}^2$, $\boldsymbol{\eta}$ is the length-$\boldsymbol{D}$ (complex-valued) harmonic, and $\boldsymbol{G}$ is a $\boldsymbol{N} \times \boldsymbol{D}$ matrix that describes all motion encoding information (e.g., directions, phase offsets, polarities, NEX). For example, in SLIM [6], $\boldsymbol{G}$ is a submatrix of the discrete Fourier transform (DFT). Let $[\widehat{\boldsymbol{m}}, \widehat{\boldsymbol{\eta}}]^T = \boldsymbol{\Psi}\{\boldsymbol{f}\}$ be any unbiased estimator of the model parameters. The CRLB is a lower bound on the covariance of $\boldsymbol{\Psi}\{\boldsymbol{f}\}$; or, an upper bound on its SNR since $\boldsymbol{\Psi}\{\boldsymbol{f}\}$ is here unbiased. For brevity, we limit our discussion to cases where $\mathbf{1}^T\boldsymbol{G}$=$\mathbf{0}$ and $\boldsymbol{G}^T\boldsymbol{G} = \mathbf{0}$, which includes most contemporary MRE protocols. Within this regime, it can be shown that the harmonic CRLB is:

$$\mathbf{COV}(\widehat{\boldsymbol{\eta}}) \geq \frac{4\sigma^2}{|m|^2}(\boldsymbol{G}^*\boldsymbol{G})^{-1} = \frac{2}{\mathrm{SNR}^2(f)}(\boldsymbol{G}^*\boldsymbol{G})^{-1} \qquad (1)$$

Since $\widehat{\boldsymbol{\eta}}$ is a phase-based statistic, it is not surprising that the minimum achievable covariance increases as raw signal SNR ($\mathrm{SNR}(\boldsymbol{f}) = |\boldsymbol{m}|/(\boldsymbol{\sigma}\sqrt{\mathbf{2}})$) decreases. The dependence on $\boldsymbol{G}$ in (1) reveals how an MEG setup impacts the limit of harmonic estimation performance. Comparing the minimum feasible covariance of $\widehat{\boldsymbol{\eta}}$ for different acquisition protocols is also straightforward given (1). Since maximum likelihood estimators (MLE) asymptotically achieve the CRLB [10], we next consider the complex harmonic MLE as defined in [11]:

$$[\widehat{\boldsymbol{m}}, \widehat{\boldsymbol{\eta}}\,] = \arg\min_{m,\eta} \sum_n |\boldsymbol{m}\exp\{\mathrm{j}\boldsymbol{Re}\{\boldsymbol{\delta}_n^T\boldsymbol{G\eta}\}\} - \boldsymbol{f}(n)|^2 \qquad (2)$$

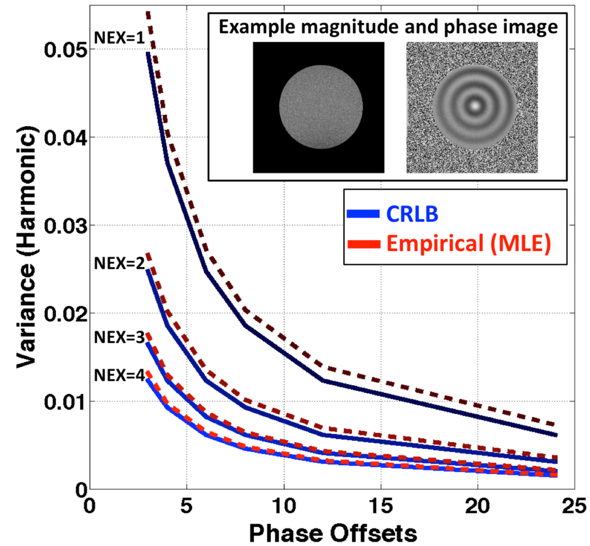

Fig. 1) Experimental harmonic estimator variance and CRLB predictions for various phase offset and NEX combinations.

After reducing the dimensionality of (2) via variable projection (VARPRO), such that it explicitly depends only on $\boldsymbol{\eta}$, it can be shown that the Hessian matrix of the cost functional, $\boldsymbol{H}$, satisfies $\boldsymbol{rank}(\boldsymbol{H}) \leq \boldsymbol{min}(\mathbf{2}\boldsymbol{D}, \boldsymbol{N} - \mathbf{1})$. Since (2) contains $\mathbf{2}\boldsymbol{D}$ real-valued unknowns after reduction, note that a (locally) unique harmonic estimate may not exist if $\boldsymbol{rank}(\boldsymbol{H}) < \mathbf{2}\boldsymbol{D}$. Therefore, $\boldsymbol{N} \geq \mathbf{2}\boldsymbol{D} + \mathbf{1}$ is required for (local) harmonic uniqueness to be feasible. Thus, for $\boldsymbol{D} = \mathbf{1}, \boldsymbol{N} \geq \mathbf{3}$ MRE measurements should be acquired; and for $\boldsymbol{D} = \mathbf{3}, \boldsymbol{N} \geq \mathbf{7}$ measurements should be acquired. Note that these sample numbers are below what is commonly used in MRE, suggesting rationalized opportunity for reducing MRE acquisition time (SNR permitting). To validate the accuracy of (1), a homogenous stiffness phantom was imaged twice at 1.5 T using a 2D GRE sequence with $\boldsymbol{D}$=1, NEX=4, and $\boldsymbol{N}$ =24 equispaced phase offsets over one driving motion cycle (60 Hz). One series was used to construct a baseline harmonic and magnitude reference, while the other was subsampled to simulate various NEX≤4 and $\boldsymbol{N}$≤24 acquisitions. For each setup, a harmonic estimate was generated via MLE (2) and its sample variance relative to baseline was recorded. The theoretical harmonic CRLB was then computed for the acquisition parameters.

Results: Fig. 1 shows the empirically measured, simulated, and theoretically predicted variance results from the phantom experiment. Lower estimator variance is desirable. That the empirical variance and CRLB estimates closely match across all NEX and phase offset pairs highlights the CRLB's accuracy at predicting experimental MRE performance. Also note that variance estimates hold down to $\boldsymbol{N} = \mathbf{3}$, which coincides with the minimum sampling requirement for monodirectional experiments.

Discussion: The benefits of a theoretical MRE performance evaluation platform based around the raw MRI signal – rather than the motion-induced phase signal – are many-fold. In addition to providing a statistically accurate model of error propagation and harmonic estimation complexity, this framework potentiates the concrete and objective comparison of existing MRE acquisition protocols (e.g., tetrahedral vs. SLIM), and can serve as a guiding tool for protocol development. This framework also provides a foundation for rigorously investigating the impact of scan nonidealities such as intravoxel phase dispersion (IVPD) [12], T_2^* effects, and concomitant fields on harmonic estimation performance. Additional possible extensions include generalization for multifrequency protocols, accelerated acquisitions, or regularized (i.e., biased) complex harmonic estimation [13].

Conclusion: The CRLB identifies the fundamental performance (estimator covariance) limits of any unbiased complex harmonic estimator, and provides an accurate and objective metric for comparing the performance potential of different steady-state MRE acquisition protocols or guiding the development of new ones. This bound, in turn, elucidates the minimum number of time samples needed to theoretically guarantee that the MRE harmonic estimation is fundamentally well-posed.

References: [1] Muthupillai et al., Science 1995:269;1854-57 [2] Manduca et al., Med Imag Anal 2001:5:237-54 [3] Wang et al., PMB 2008:53;2181-96 [4] Rump et al., MRM 2007:57;388-95 [5] Pelc et al., JMRI 1991:1;405-13 [6] Klatt et al., PMB 2013:58;8663-75 [7] Nir et al., MRM in press;DOI:10.1002/mrm.25280 [8] McGarry et al., PMB 2011:56;153-64 [9] Gudbjartsson and Patz, MRM 1995:34;910-4 [10] Kay, Fundamentals of Statistical Signal Processing Vol. I, 1993 [11] Trzasko and Manduca, ISMRM 2012:3425 [12] Glaser et al., MRM 2003:50;1256-65 [13] Trzasko et al., ISMRM 2014:4268