The Cramér-Rao Bound and Its Application to Quantification in MRS

Qiang Ning

Department of Electrical and Computer Engineering Beckman Institute for Advanced Science and Techonology University of Illinois at Urbana-Champaign

Abstract

Cramer-Rao Bound (CRB) is an important inequality on the error correlation matrix of an estimator. It describes the theoretical lower bound for an estimator (usually unbiased). Therefore, it is a useful index of how efficiently an estimator is. Here we will summarize the derivation of CRB, list some examples and apply this analysis to the quantification (parameters estimation) of spin-echo signals in MRI.

I. CRAMER-RAO BOUND

This section and the following examples section are essentially based on Levy's book *Principles of signal detection and parameter estimation* [1].

A. Definition

Let the parameters of an estimator be an m dimensional vector x, and the measurement data be an n dimensional vector Y. The estimator here is denoted by $\hat{X}(Y)$. The Cramer-Rao Bound that we usually used for unbiased estimators is

$$C_E(x) \ge J^{-1}(x),\tag{1}$$

where

$$C_E(x) = E[(x - \hat{X}(Y))(x - \hat{X}(Y))^T]$$
(2)

is the error correlation matrix of X, and

$$J(x) = E_Y[\nabla_x \ln f_Y(Y|x)(\nabla_x \ln f_Y(Y|x))^T],$$
(3)

or equivalently (which is proved in [1]),

$$J(x) = -E_Y[\nabla_x \nabla_x^T \ln f_Y(Y|x)], \tag{4}$$

is the so-called Fisher Information in Y about the parameters in X. Note in (3) and (4), $f_Y(Y|X)$ is the conditional probability distribution function of measurement Y on parameters X, and the gradient operator is defined as

$$\nabla_x = \begin{bmatrix} \frac{\partial}{\partial x_1} & \frac{\partial}{\partial x_2} & \cdots & \frac{\partial}{\partial x_m} \end{bmatrix}^T.$$
 (5)

In practice, the Fisher Information can be calculated entry-wisely in the following two ways.

$$J_{i,j}(x) = E_Y \left[\frac{\partial}{\partial x_i} \ln f_Y(Y|x) \frac{\partial}{\partial x_j} \ln f_Y(Y|x)\right]$$

= $-E_Y \left[\frac{\partial^2}{\partial x_i \partial x_j} \ln f_Y(Y|x)\right].$ (6)

Given this bound, we have the estimator variance of each parameter,

$$E[(x_i - \hat{x}_i(Y))^2] \ge [J^{-1}]_{ii}(x), \tag{7}$$

which is useful in the analysis of the efficiency of an estimator.

B. Proof

We prove a more generalized form:

$$C_E(x) \ge b(x)b^T(x) + (I_m - \nabla_X^T b(x))J^{-1}(x)(I_m - \nabla_X^T b(x))^T,$$
(8)

where b(x) is the bias of this estimator,

$$b(x) = x - E(\hat{X}(Y)).$$
 (9)

It is obvious that when the estimator is unbiased, that is, b(x) = 0, (8) degenerates to (1).

Form a 2m dimensional vector

$$Z = \begin{bmatrix} x - \hat{X}(Y) - b(x) \\ \nabla_x \ln(f_Y(Y|x)) \end{bmatrix}.$$
(10)

Then let

$$C_{Z} = E[ZZ^{T}] = \begin{bmatrix} C_{11} & C_{12} \\ C_{21} & C_{22} \end{bmatrix}$$
(11)

be its correlation matrix. From (2) and (3), we can immediately have

$$C_{11} = C_E(x) - b(x)b^T(x),$$
(12)

$$C_{22} = J(x).$$
 (13)

It remains to evaluate

$$C_{21}^{T} = C_{12} = E[(x - \hat{X}(Y) - b(x)) \bigtriangledown^{T}_{X} \ln(f_{Y}(Y|x))]$$

= $\int (x - \hat{X}(y) - b(x)) \bigtriangledown^{T}_{x} (f_{Y}(y|x)) dy.$ (14)

Note

$$0 = \nabla_{x}^{T} \{ [x - \hat{X}(y) - b(x)] f_{Y}(y|x) \}$$

= $f_{Y}(y|x) \nabla_{x}^{T} [x - \hat{X}(y) - b(x)] + [x - \hat{X}(y) - b(x)] \nabla_{x}^{T} f_{Y}(y|x)$
= $f_{Y}(y|x) [I_{m} - \nabla_{x}^{T} b(x)] + [x - \hat{X}(y) - b(x)] \nabla_{x}^{T} f_{Y}(y|x).$ (15)

Integrating this identity with respect to y gives

$$C_{12} = -I_m + \nabla_x^T b(x). \tag{16}$$

Assuming the information matrix $C_{22} = J(x)$ is positive definite (i.e., invertible, which is usually true) at point X, we can perform Schur decomposition to $C_Z(x)$:

$$\begin{pmatrix} C_{11} & C_{12} \\ C_{21} & C_{22} \end{pmatrix} = \begin{pmatrix} I_m & C_{12}C_{22}^{-1} \\ 0 & I_m \end{pmatrix} \begin{pmatrix} C_{11} - C_{12}C_{22}^{-1}C_{21} & 0 \\ 0 & C_{22} \end{pmatrix} \begin{pmatrix} I_m & 0 \\ C_{22}^{-1}C_{21} & I_m \end{pmatrix}.$$

Because the correlation matrix $C_Z(x) \ge 0$, $C_{11} - C_{12}C_{22}^{-1}C_{21}$ is also non-negative definite, i.e.,

$$C_E(x) - b(x)b^T(x) - (I_m - \nabla_x^T b(x))J^{-1}(x)(I_m - \nabla_x^T b(x))^T \ge 0,$$
(17)

which is exactly (8).

		ъ	
		л	

C. Example

1) CRB Calculation: Consider the estimation of the mean and variance of a sequence $\{Y_k, 1 \le k \le N\}$ of i.i.d. N(m, v) gaussian random variables.

$$f_Y(y_k|m,v) = \frac{1}{\sqrt{2\pi v}} e^{-\frac{(y_k-m)^2}{2v}}, k = 1, 2, \dots, N,$$
$$f_Y(\mathbf{y}|m,v) = \frac{1}{(\sqrt{2\pi v})^N} e^{-\frac{\sum_{k=1}^N (y_k-m)^2}{2v}},$$
$$L(\mathbf{y}|m,v) = \ln(f_Y(\mathbf{y}|m,v)) = -\frac{N}{2} \ln(2\pi v) - \frac{1}{2v} \sum_{k=1}^N (y_k-m)^2.$$

First order derivatives are

$$\frac{\partial L}{\partial m} = \frac{1}{v} \sum_{k=1}^{N} (y_k - m), \tag{18}$$

and

$$\frac{\partial L}{\partial v} = -\frac{N}{2v} + \frac{1}{2v^2} \sum_{k=1}^{N} (y_k - m)^2.$$
(19)

Then second derivatives are

$$\frac{\partial^2 L}{\partial m^2} = -\frac{N}{v},$$
$$\frac{\partial^2 L}{\partial v^2} = \frac{N}{2v^2} - \frac{1}{v^3} \sum_{k=1}^N (y_k - m)^2,$$

and

$$\frac{\partial^2 L}{\partial m \partial v} = -\frac{1}{v^2} \sum_{k=1}^N (y_k - m).$$

Therefore the Fisher Information matrix is

$$J(m,v) = N \begin{pmatrix} v^{-1} & 0\\ 0 & (2v^2)^{-1} \end{pmatrix},$$
(20)

$$J^{-1}(m,v) = N^{-1} \begin{pmatrix} v & 0\\ 0 & 2v^2 \end{pmatrix}.$$
 (21)

Then the error variances of the entries of any unbiased estimator must satisfy

$$E[(m - \hat{m}(Y))^2] \geq \frac{v}{N}, \tag{22}$$

$$E[(v - \hat{v}(Y))^2] \ge \frac{2v^2}{N}.$$
 (23)

2) Efficiency: An unbiased estimator is efficient if it reaches its CRB, which means $C_E(X) - J^{-1}(X) = 0$. Further if only a partial of the eigenvalues of $C_E(X) - J^{-1}(X)$ is zero, it is called partially efficient.

By setting (18) and (19) to be zero, we have

$$\hat{m}_{ML}(Y) = \frac{1}{N} \sum_{k=1}^{N} y_k,$$
(24)

and

$$\hat{v}_{ML}(Y) = \frac{1}{N} \sum_{k=1}^{N} (y_k - \hat{m})^2.$$
(25)

It is proved in [1] that

$$E[\hat{m}_{ML}(Y)] = m, (26)$$

$$E[\hat{v}_{ML}(Y)] = \frac{N-1}{N}v,$$
 (27)

$$E[(m - \hat{m}_{ML}(Y))^2] = \frac{v}{N},$$
(28)

$$E[(v - \hat{v}_{ML}(Y))^2] = \frac{2N - 1}{N^2}v^2.$$
(29)

From the results we see that the unbiased estimator $\hat{m}_{ML}(Y)$ is efficient because it reaches its CRB as defined in (21). Even though the estimator $\hat{v}_{ML}(Y)$ is biased, its error variance, however, is smaller than the CRB for unbiased estimators. This implies that it is not necessary that biased estimators have poor error variance performances, instead allowing a small bias can sometimes be benificial.

Another fact mentioned in [1] on pp. 145 is that all ML estimators have these two properties:

- 1) Asymptotically unbiased, i.e., $\lim_{N\to\infty} b(X) = 0$;
- 2) Asymptotically efficient, i.e., $\lim_{N\to\infty} E[(x_i \hat{x}_i(Y))^2] = [J^{-1}]_{ii}(X);$

which can be seen from the example above.

II. QUANTIFICATION OF SINGLE SPIN-ECHO SIGNALS

A. Formulation

We use the model that introduced in Chap. 5.2 *Proposed formulation* [2], ignoring baseline signals.

$$s[m] = s_{metab}[m] + \xi[m], \qquad (30)$$

$$s_{metab}[m] = e^{i\phi_0} \sum_{n=1}^{N} a_n(TE)\varphi_{n,TE}[m]\psi_{n,d_n}[m], \qquad (31)$$
$$m = 0, 1, \dots, M-1,$$

where $\xi[m] \sim N(0, \sigma^2)$ is a complex gaussian noise, ϕ_0 is a zero-order term phase, $a_n(TE)$ is a real positive amplitude assumed to exponentially decay with respect to TE

$$a_n(TE) = c_n e^{-TE/T_{2,n}}, (32)$$

and $\varphi_{n,TE}[m]$ and $\psi_{n,d_n}[m]$ are metabolite basis function and signal decay, respectively, defined as

$$\varphi_{n,TE}[m] = \sum_{l=1}^{L_n} \alpha_{l,n}(TE) e^{-i\beta_{l,n}(TE)} e^{-i2\pi f_{l,n}(TE)m\Delta t},$$
(33)

$$\psi_{n,d_n}[m] = e^{-m\Delta t/d_n}. \tag{34}$$

In the above formulations, $T_{2,n}$ is a metabolite-dependent relaxation constant, d_n is a real lineshape parameter and Δt is the sampling time. $\alpha_{l,n}(TE)$, $\beta_{l,n}(TE)$ and $f_{l,n}(TE)$ are relative amplitude, phase and frequency of the *l*-th resonance of the *n*-th metabolite which can all be determined from quantum mechanical simulations.

The parameter vector that we are going to estimate is

$$\theta = [a_1, \dots, a_N, d_1, \dots, d_N, \phi_0]^T.$$
(35)

B. Entrywise Derivation of CRB

The probability distribution function of an *n*-channel i.i.d. real gaussian variable $X \sim N(0, \sigma^2 I_n)$, $X \in \mathbb{C}^n$ is

$$f_X(x) = \frac{1}{(2\pi\sigma^2)^{n/2}} e^{-\frac{\|x\|^2}{2\sigma^2}}.$$
(36)

The likelihood function of $s[m], m = 0, \dots, M - 1$ is therefore

$$L(s[m]) = \frac{1}{(\pi\sigma^2)^M} e^{-\frac{|\xi[m]|^2}{\sigma^2}},$$

$$\ln L(s[m]) = \operatorname{const} - \frac{1}{\sigma^2} \sum_{m=0}^{M-1} |\xi[m]|^2,$$
(37)

where $\xi[m] \sim N(0, \sigma^2)$. Using the result that $\frac{\partial ||z||^2}{\partial \alpha} = z(\frac{\partial z^*}{\partial \alpha}) + z^*(\frac{\partial z}{\partial \alpha}) = 2Re\{z(\frac{\partial z^*}{\partial \alpha})\}$ where $z \in \mathbb{C}, \ \alpha \in \mathbb{R}$, we have

$$\frac{\partial \ln L}{\partial \theta_k} = -\frac{1}{\sigma^2} \sum_{m=0}^{M-1} \left\{ \xi[m] \frac{\partial \xi^*[m]}{\partial \theta_k} + \xi^*[m] \frac{\partial \xi[m]}{\partial \theta_k} \right\},\tag{38}$$

where

$$\xi^{*}[m] = s^{*}[m] - e^{-i\phi_{0}} \sum_{n=1}^{N} a_{n}(TE)\varphi^{*}_{n,TE}[m]\psi^{*}_{n,d_{n}}[m],$$

$$\left(\frac{\partial\xi[m]}{\partial a_k}\right)^* = \frac{\partial\xi^*[m]}{\partial a_k} = -e^{-i\phi_0}\varphi^*_{k,TE}[m]\psi^*_{k,d_k}[m],$$
(39)

$$\frac{\partial \xi[m]}{\partial d_k})^* = \frac{\partial \xi^*[m]}{\partial d_k} = -e^{-i\phi_0} a_k(TE) \varphi^*_{k,TE}[m] \frac{\partial \psi^*_{k,d_k}[m]}{\partial d_k}, \tag{40}$$

$$\frac{\partial \xi[m]}{\partial \phi_0})^* = \frac{\partial \xi^*[m]}{\partial \phi_0} = ie^{-i\phi_0} \sum_{n=1}^N a_n(TE)\varphi_{n,TE}^*[m]\psi_{n,d_n}^*[m], \qquad (41)$$

$$k = 1, 2, \dots, N.$$

By (6), we have

(

$$F_{p,q}(\theta) = E_{\xi} \left[\left(\frac{\partial \ln L}{\partial \theta_p} \right) \left(\frac{\partial \ln L}{\partial \theta_q} \right) \right]$$
(42)

In calculating that, we will need the expectation of $\xi^*[m_1]\xi[m_2]$ and $\xi[m_1]\xi[m_2]$, $\forall m_1, m_2 = 1, \ldots, M$. Because the gaussian noise channels are i.i.d., it is easy to get

$$E_{\xi}\{\xi^{*}[m_{1}]\xi[m_{2}]\} = \begin{cases} \sigma^{2}, \text{ for } m_{1} = m_{2} \\ 0, \text{ for } m_{1} \neq m_{2} \end{cases}$$

$$E_{\xi}\{\xi[m_{1}]\xi[m_{2}]\} = 0, \text{ for } m_{1} \neq m_{2}.$$
(43)

To handle $\xi[m]\xi[m]$, we firstly decompose it into real variables:

$$\xi[m] = \xi_r[m] + i\xi_i[m], \tag{44}$$

where $\xi_r[m], \xi_i[m] \sim N(0, \frac{\sigma^2}{2})$ and are independent with each other. And then

$$E_{\xi}\{\xi[m]\xi[m]\} = E_{\xi}\{\xi_r^2 + 2i\xi_r\xi_i - \xi_i^2\} = E_{\xi}\{\xi_r^2 - \xi_i^2\} = 0.$$
(45)

Therefore

$$E_{\xi}\{\xi[m_1]\xi[m_2]\} = 0, \forall m_1, m_2 = 1, \dots, M.$$
(46)

Taking (43) and (46) into consideration, the entries of the Fisher Information matrix is

$$F_{p,q}(\theta) = \frac{1}{\sigma^4} E_{\xi} \left\{ \sum_{m_1=0}^{M-1} \left[\xi[m_1] \frac{\partial \xi^*[m_1]}{\partial \theta_p} + \xi^*[m_1] \frac{\partial \xi[m_1]}{\partial \theta_p} \right] \right\}$$

$$= \sum_{m_2=0}^{M-1} \left[\xi[m_2] \frac{\partial \xi^*[m_2]}{\partial \theta_q} + \xi^*[m_2] \frac{\partial \xi[m_2]}{\partial \theta_q} \right] \right\}$$

$$= \frac{1}{\sigma^4} E_{\xi} \left\{ \sum_{m=0}^{M-1} \left[\xi[m] \xi^*[m] \frac{\partial \xi^*[m]}{\partial \theta_p} \frac{\partial \xi[m]}{\partial \theta_q} + \xi^*[m] \xi[m] \frac{\partial \xi[m]}{\partial \theta_p} \frac{\partial \xi^*[m]}{\partial \theta_q} \right] \right\}$$

$$= \frac{1}{\sigma^2} \sum_{m=0}^{M-1} \left[\frac{\partial \xi^*[m]}{\partial \theta_p} \frac{\partial \xi[m]}{\partial \theta_q} + \frac{\partial \xi[m]}{\partial \theta_p} \frac{\partial \xi^*[m]}{\partial \theta_q} \right]$$

$$= \frac{2}{\sigma^2} \sum_{m=0}^{M-1} Re \left\{ \frac{\partial \xi^*[m]}{\partial \theta_p} \frac{\partial \xi[m]}{\partial \theta_q} \right\}.$$
(47)
(48)

Substituting (39)(40)(41) into (47), we get for $\forall p, q = 1, \dots, N$

$$\begin{aligned} F_{a_{p},a_{q}}(\theta) &= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re\left\{ \frac{\partial \xi^{*}[m]}{\partial a_{p}} \frac{\partial \xi[m]}{\partial a_{q}} \right\} \\ &= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re\left\{ -e^{-i\phi_{0}} \varphi_{p,TE}^{*}[m] \psi_{p,d_{p}}^{*}[m](-e^{i\phi_{0}} \varphi_{q,TE}[m]) \psi_{q,d_{q}}[m]) \right\} \\ &= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re\left\{ \varphi_{p,TE}^{*}[m] \psi_{p,d_{p}}^{*}[m] \varphi_{q,TE}[m] \psi_{q,d_{q}}[m] \right\}, \end{aligned}$$
(49)
$$F_{d_{p},d_{q}}(\theta) &= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re\left\{ \frac{\partial \xi^{*}[m]}{\partial d_{p}} \frac{\partial \xi[m]}{\partial d_{q}} \right\} \\ &= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re\left\{ a_{p}a_{q}\varphi_{p,TE}^{*}[m] \frac{\partial \psi_{p,d_{p}}[m]}{\partial d_{p}} \varphi_{q,TE}[m] \frac{\partial \psi_{q,d_{q}}[m]}{\partial d_{q}} \right\}, \end{aligned}$$
(50)
$$F_{\phi_{0},\phi_{0}}(\theta) &= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re\left\{ \frac{\partial \xi^{*}[m]}{\partial \phi_{0}} \frac{\partial \xi[m]}{\partial \phi_{0}} \right\} \\ &= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re\left\{ \sum_{n_{1}=1}^{N} a_{n_{1}}\varphi_{n_{1},TE}^{*}[m] \psi_{n_{1},d_{n_{1}}}^{*}[m] \right\} \end{aligned}$$

$$= \frac{2}{\sigma^2} \sum_{m=0}^{M-1} Re \left\{ \sum_{n_1=1}^{N} \sum_{n_2=1}^{N} a_{n_1} a_{n_2} \varphi_{n_1,TE}^*[m] \psi_{n_1,d_{n_1}}^*[m] \varphi_{n_2,TE}[m] \psi_{n_2,d_{n_2}}[m] \right\}, (51)$$

$$F_{a_p,d_q}(\theta) = \frac{2}{\sigma^2} \sum_{m=0}^{M-1} Re \left\{ \frac{\partial \xi^*[m]}{\partial a_p} \frac{\partial \xi[m]}{\partial d_q} \right\}$$

$$= \frac{2}{\sigma^2} \sum_{m=0}^{M-1} Re \left\{ a_q \varphi_{p,TE}^*[m] \psi_{p,d_p}^*[m] \varphi_{q,TE}[m] \frac{\partial \psi_{q,d_q}[m]}{\partial d_q} \right\},$$
(52)

$$F_{a_{p},\phi_{0}}(\theta) = \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re \left\{ \frac{\partial \xi^{*}[m]}{\partial a_{p}} \frac{\partial \xi[m]}{\partial \phi_{0}} \right\}$$

$$= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re \left\{ i\varphi_{p,TE}^{*}[m]\psi_{p,d_{p}}^{*}[m] \sum_{n=1}^{N} a_{n}\varphi_{n,TE}[m]\psi_{n,d_{n}}[m] \right\}$$

$$= -\frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Im \left\{ \varphi_{p,TE}^{*}[m]\psi_{p,d_{p}}^{*}[m] \sum_{n=1}^{N} a_{n}\varphi_{n,TE}[m]\psi_{n,d_{n}}[m] \right\},$$
(53)

$$F_{d_{p},\phi_{0}}(\theta) = \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re \left\{ \frac{\partial \xi^{*}[m]}{\partial d_{p}} \frac{\partial \xi[m]}{\partial \phi_{0}} \right\}$$

$$= \frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Re \left\{ ia_{p} \varphi^{*}_{p,TE}[m] \frac{\partial \psi^{*}_{p,d_{p}}[m]}{\partial d_{p}} \sum_{n=1}^{N} a_{n} \varphi_{n,TE}[m] \psi_{n,d_{n}}[m] \right\}$$

$$= -\frac{2}{\sigma^{2}} \sum_{m=0}^{M-1} Im \left\{ a_{p} \varphi^{*}_{p,TE}[m] \frac{\partial \psi^{*}_{p,d_{p}}[m]}{\partial d_{p}} \sum_{n=1}^{N} a_{n} \varphi_{n,TE}[m] \psi_{n,d_{n}}[m] \right\}.$$
(54)

Here we have got the entries of $F_{p,q}(\theta)$ above its diagonal, and the rest of the entries are the conjugate transpose of the upper triangular part.

$$F(\theta) = \begin{pmatrix} F_{a,a} & F_{a,d} & F_{a,\phi_0} \\ F_{a,d}^H & F_{d,d} & F_{d,\phi_0} \\ F_{a,\phi_0}^H & F_{d,\phi_0}^H & F_{\phi_0,\phi_0} \end{pmatrix}.$$
 (55)

C. Matrix Derivation of CRB

In deriving the CRB entrywisely, we see the formulations are much complicated due to a large number of summations. If we utilize matrix derivatives, the labor can be greatly reduced.

Rewrite the signal model in matrix form.

$$\mathbf{s} = e^{i\phi_0} \mathbf{Z} \mathbf{a} + \xi, \tag{56}$$

where $\mathbf{Z}_{m,n} = \varphi_{n,TE}[m]\psi_{d,d_n}[m], \ m = 0, \dots, M - 1, \ n = 1, \dots, N$ and

$$\mathbf{s} = \begin{pmatrix} s[0] \\ s[1] \\ \vdots \\ s[M-1] \end{pmatrix}, \mathbf{a} = \begin{pmatrix} a_1 \\ a_2 \\ \vdots \\ a_N \end{pmatrix}, \mathbf{d} = \begin{pmatrix} d_1 \\ d_2 \\ \vdots \\ d_N \end{pmatrix}, \boldsymbol{\xi} = \begin{pmatrix} \boldsymbol{\xi}[0] \\ \boldsymbol{\xi}[1] \\ \vdots \\ \boldsymbol{\xi}[M-1] \end{pmatrix}.$$
 (57)

I will not keep these variables bold face hereafter for simplicity. Then the likelihood function is

$$\ln L(s) = \text{const} - \frac{1}{\sigma^2} \|\xi\|^2.$$
 (58)

According to my previous weekly summary (week 12) of the gradient calculation of least squares problems, we have

$$\nabla_{\theta} \ln L = -\frac{1}{\sigma^2} (J^H \xi + (J^H \xi)^*), \tag{59}$$

where J is the jacobian matrix of ξ over θ (denote the Fisher Information matrix by another notation F to avoid conflict).

$$J = \frac{\partial \xi}{\partial \theta}$$

= $\begin{bmatrix} \frac{\partial \xi}{\partial a} & \frac{\partial \xi}{\partial d} & \frac{\partial \xi}{\partial \phi_0} \end{bmatrix}$
= $\begin{bmatrix} -e^{i\phi_0}Z & -e^{i\phi_0}DA & -ie^{i\phi_0}Za \end{bmatrix},$ (60)

where

$$D = \begin{bmatrix} \frac{\partial Z_1}{\partial d_1} & \dots & \frac{\partial Z_N}{\partial d_N} \end{bmatrix},$$

$$A = \begin{pmatrix} a_1 & 0 & \cdots & 0 \\ 0 & a_2 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & a_N \end{pmatrix}.$$
(61)
$$(62)$$

By (3) and (59), we have

$$F = E\left\{ \left(\bigtriangledown_{\theta} \ln L \right) \left(\bigtriangledown_{\theta} \ln L \right)^{H} \right\}$$

$$= \frac{1}{\sigma^{4}} E\left\{ \left(J^{H} \xi + \left(J^{H} \xi \right)^{*} \right) \left(\xi^{H} J + \left(\xi^{H} J \right)^{*} \right) \right\}$$

$$= \frac{2}{\sigma^{2}} Re\{J^{H} J\}.$$
(63)

Using (60), we have

$$F_{a,a}(\theta) = \frac{2}{\sigma^2} Re\{Z^H Z\},$$
(64)

$$F_{d,d}(\theta) = \frac{2}{\sigma^2} Re\{A^H D^H DA\},$$
(65)

$$F_{\phi_0,\phi_0}(\theta) = \frac{2}{\sigma^2} Re\{a^H Z^H Za\},\tag{66}$$

$$F_{a,d}(\theta) = \frac{2}{\sigma^2} Re\{Z^H DA\},$$
(67)

$$F_{a,\phi_0}(\theta) = -\frac{2}{\sigma^2} Im\{Z^H Za\},$$
(68)

$$F_{d,\phi_0}(\theta) = -\frac{2}{\sigma^2} Im\{A^H D^H Za\}.$$
(69)

Finally

$$F(\theta) = \begin{pmatrix} F_{a,a} & F_{a,d} & F_{a,\phi_0} \\ F_{a,d}^H & F_{d,d} & F_{d,\phi_0} \\ F_{a,\phi_0}^H & F_{d,\phi_0}^H & F_{\phi_0,\phi_0} \end{pmatrix}.$$
(70)
REFERENCES

- [1] B. C. Levy, Principles of signal detection and parameter estimation. Springer, 2008, ch. 4.4, pp. 131-150.
- [2] H. M. Nguyen, "Towards high-resolution magnetic resonance spectroscopic imaging: Spatiotemporal denoising and echotime selection," Ph.D. dissertation, University of Illinois at Urbana-Champaign, 2011.