

# Synthetic MR : Optimal Experimental Design

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## Introduction

### Problem Statement

Consider a magnetization signal  $M_{TD}$  that is defined as

$$M_{TD}(\mathcal{K}, \mathcal{P}, \mathbf{x}) = \left( M_0(\mathbf{x}) \frac{1 - (1 - \cos \theta) e^{-\frac{T_D}{T_1(\mathbf{x})}} - \cos \theta e^{-\frac{T_D}{T_1(\mathbf{x})}}}{1 - \cos \theta e^{-\frac{T_R}{T_1(\mathbf{x})}} \cos \alpha} \right) e^{-\frac{T_E}{T_2(\mathbf{x})}} \quad (1)$$

where,  $M_0$  is the unsaturated magnetization,  $\theta$  represents the flip angle, and  $T_R$  and  $T_E$  denote repetition time and echo time, respectively. Parameters  $T_1$  and  $T_2$  represents relaxation times, and  $\alpha$  is the excitation pulse. Note that the unsaturated magnetization  $M_0$ , along with relaxation times  $T_1$  and  $T_2$ , are a function of spatial coordination  $\mathbf{x}$ . As well, excitation pulse  $\alpha$  is a function of flip angle in general, i.e.  $\alpha = \alpha(\theta)$ .

In practice, the MRI observations are Fourier transform of  $M_{TD}$ , usually polluted with a white noise  $\nu$  (with mean zero and variance  $\mathbf{R}$ ). Hence, Eq. (1) can be written as:

$$z(\mathcal{K}, \mathcal{P}) = \underbrace{M_{TD}(\mathcal{K}, \mathcal{P}, \mathbf{x}) e^{-j\Delta\omega_0(\mathbf{x})}}_{h(\mathcal{K}, \mathcal{P})} + \nu \quad (2)$$

Note that the observation  $z$  is a function of control parameters  $\mathcal{K} = \{T_R, T_D, \theta, T_E\}$  and parameters of interest  $\mathcal{P}$ . The ultimate goal is to provide accurate estimate of the parameters  $\mathcal{P} \equiv \{T_1, T_2, M_0\}$ , given some measurements  $z$ .

Precise estimation of parameters  $\mathcal{P}$  crucially depends on the values of control parameters  $\mathcal{K} = \{T_R, T_D, \theta, T_E\}$ . In other words, to ensure performance of the estimation algorithm, one needs to select the control parameters  $\mathcal{K} = \{T_R, T_D, \theta, T_E\}$  such that the observation  $z$  provides useful information about the parameters  $\mathcal{P}$ . This is achieved by maximizing the mutual information between the control parameters  $\mathcal{K}$  and parameters of interest  $\mathcal{P}$ .

## Optimal Experimental Design

As discussed before, performance of estimation process crucially depends on the value of control parameters  $\mathcal{K}$ . Hence, it is important to develop mathematical tools to identify the control parameters  $\mathcal{K}$  such that they provide the best observation data for accurate estimation of parameter  $\mathcal{P}$ . This is equivalent with maximizing the mutual information between the observation data and parameters  $\mathcal{P}$ . Based on information theory, mutual information is defined as the reduction of uncertainty in one parameter due to knowledge of the other parameter.

$$I(\mathcal{P}; z) = \int_z \int_{\mathcal{P}} p(\mathcal{P}, z) \ln \left( \frac{p(\mathcal{P}, z)}{p(\mathcal{P})p(z)} \right) d\mathcal{P} dz \quad (3)$$

We make use of Bayes theorem to simplify the above equation. By substituting  $p(\mathcal{P}, z)$  with  $p(z|\mathcal{P})p(\mathcal{P})$ , Eq. (3) can be written as:

$$I(\mathcal{P}; z) = \int_z \int_{\mathcal{P}} p(z|\mathcal{P})p(\mathcal{P}) \ln \left( \frac{p(z|\mathcal{P})p(\mathcal{P})}{p(\mathcal{P})p(z)} \right) d\mathcal{P} dz \quad (4)$$

Or,

$$I(\mathcal{P}; z) = \int_z \int_{\mathcal{P}} p(z|\mathcal{P})p(\mathcal{P}) \ln [p(z|\mathcal{P})] d\mathcal{P}dz - \int_z p(z) \ln p(z)dz \quad (5)$$

Note that due to dependence of observation data  $z$  on control parameters, the mutual information  $I(\mathcal{P}; z)$  is a function of control parameter  $\mathcal{K}$ . In order to maximize the reduction of uncertainty in parameter estimate (i.e. to have the most confident estimates of the parameter  $\mathcal{P}$ ), one can simply maximize the mutual information between the observation data and parameters of interest:

$$\max_{\mathcal{K}} I(\mathcal{P}; z) \quad (6)$$

The above maximization results in *optimal* values of control parameter  $\mathcal{K}$  for accurate estimation of parameter  $\mathcal{P}$ . Note that in Eq. (5),  $p(z|\mathcal{P})$  is defined as a Gaussian distribution with mean  $h(\mathcal{K}, \mathcal{P})$  and variance  $\mathbf{R}$ . As well,  $p(\mathcal{P})$  denotes the prior distribution of parameter  $\mathcal{P}$ , which for the ease of calculations, is considered to be a Gaussian distribution with some prior mean  $\hat{\mathcal{P}}^-$  and prior covariance  $\Sigma^-$ , i.e.  $p(\mathcal{P}) \sim \mathcal{N}(\hat{\mathcal{P}}^-, \Sigma^-)$ . Method of quadrature points can be used to evaluate Eq. (5).

We emphasize here that the mutual information will be the same on different pixels with the same tissue types. This is due to the similarities in statistics of  $\mathcal{P}$  between the two different pixels with the same tissue properties. In other words, whenever two different pixels have the same tissue properties, then the distribution of parameter  $\mathcal{P}$ , denoted by  $p(\mathcal{P})$ , is the same and so is the value of mutual information. Hence, there is no need to evaluate the mutual information for each pixel in a region with the same tissue type.

On the other hand, in a case that the tissue properties for each pixel are different from the other, then the mutual information needs to be evaluated for each and every pixel of interest.

## Model - Data Fusion

After finding the optimal values of the control parameter  $\mathcal{K}$ , we can proceed and perform the model-data fusion to get a better understanding about the uncertainties involved in parameters  $\mathcal{P}$ . The fusion of observational data with mathematical model predictions promises to provide greater understanding of physical phenomenon than either approach alone can achieve. In here, a minimum variance framework is being used for model - data fusion. Based on minimum variance technique, posterior statistics of parameter  $\mathcal{P}$  can be written as:

$$\hat{\mathcal{P}}^+ = \hat{\mathcal{P}}^- + \mathbf{K}[z - \underbrace{\mathcal{E}^-[h(\mathcal{K}, \mathcal{P})]}_{h^-}] \quad (7)$$

$$\Sigma^+ = \Sigma^- + \mathbf{K}\Sigma_{hh}\mathbf{K}^T \quad (8)$$

where, the gain matrix  $\mathbf{K}$  is given by

$$\mathbf{K} = \Sigma_{\mathcal{P}z} (\Sigma_{hh}^- + \mathbf{R})^{-1} \quad (9)$$

Here,  $\hat{\mathcal{P}}^-$  and  $\hat{\mathcal{P}}^+$  represent prior and posterior values of the mean for parameter vector  $\mathcal{P}$ , respectively:

$$\hat{\mathcal{P}}^- \equiv \mathcal{E}^-[ \mathcal{P} ] = \int \mathcal{P}^- p(\mathcal{P}) d\mathcal{P} \hat{\mathcal{P}}^+ \equiv \mathcal{E}^+[ \mathcal{P} ] = \int \mathcal{P}^+ p(\mathcal{P}) d\mathcal{P} \quad (10)$$

where,  $p(\mathcal{P})$  denotes the probability density function of parameter  $\mathcal{P}$ . Similarly, the prior and posterior covariance matrices  $\Sigma^-$  and  $\Sigma^+$  can be written as:

$$\Sigma^- \equiv \mathcal{E}[(\mathcal{P} - \hat{\mathcal{P}}^-)(\mathcal{P} - \hat{\mathcal{P}}^-)^T] \quad (11)$$

$$\Sigma^+ \equiv \mathcal{E}[(\mathcal{P} - \hat{\mathcal{P}}^+)(\mathcal{P} - \hat{\mathcal{P}}^+)^T] \quad (12)$$

The matrices  $\Sigma_{\mathcal{P}z}$  and  $\Sigma_{hh}$  are defined as:

$$\Sigma_{\mathcal{P}z} \equiv \mathcal{E}[(\mathcal{P} - \hat{\mathcal{P}})(h - \hat{h}^-)^T] \quad (13)$$

$$\Sigma_{hh} \equiv \mathcal{E}[(h - \hat{h}^-)(h - \hat{h}^-)^T] \quad (14)$$

Eq. (7) along with Eq. (8) provide posterior mean and covariance of parameter  $\mathcal{P}$  given observation data  $\tilde{z}$  and model predictions  $h(\mathcal{K}, \mathcal{P})$ . We emphasize here that the optimal values of  $\mathcal{K}$ , obtained from Eq. (6), are used in Eq. (7).

# Overall Picture

The following diagram illustrates the general work-flow of the process:

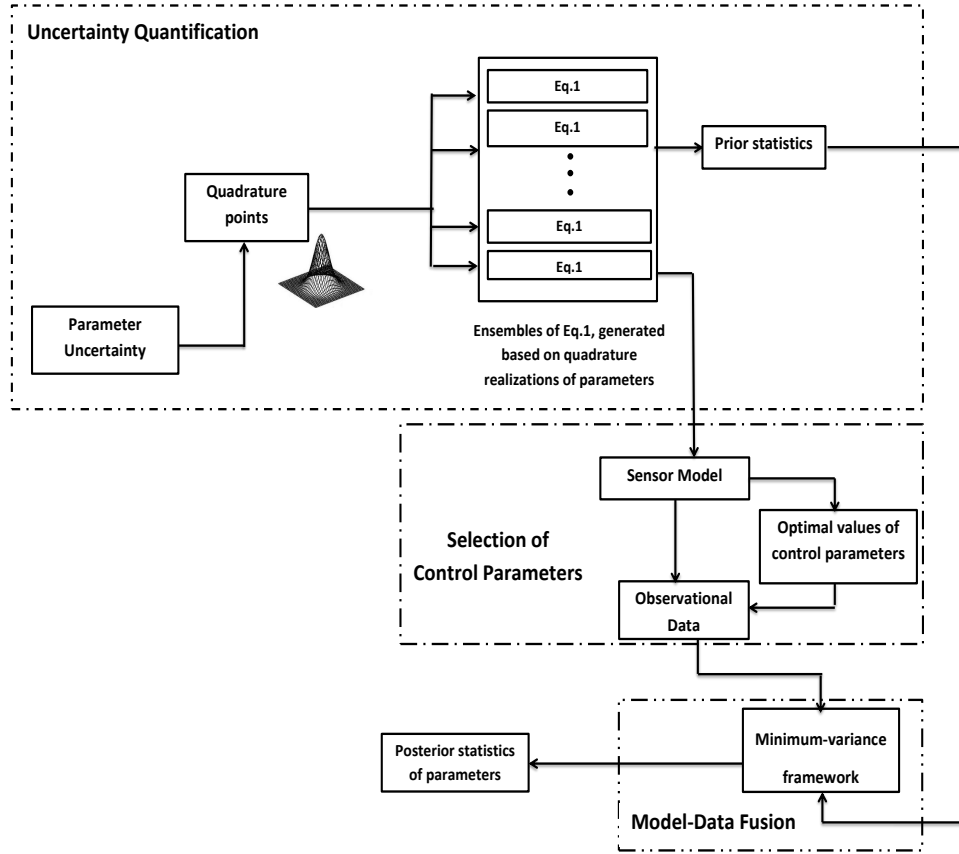


Figure 1: Schematic view of the estimation process