

# Advanced Appliations of Synthetic MR and MAGiC

March 16, 2016

## 1 Physics Model

The steady-state magnetization  $M_{TD}$  at a specific delay time  $T_D$  can be found as a function of flip angle  $\theta$ , repetition time  $T_R$ , excitation pulse  $\alpha$ , and relaxation time  $T_1$ :

$$M_{TD} = M_0 \frac{1 - (1 - \cos(\theta))e^{-\frac{T_D}{T_1}} - \cos(\theta)e^{-\frac{T_R}{T_1}}}{1 - \cos(\theta)e^{-\frac{T_R}{T_1}} \cos(\alpha)}$$

where,  $M_0$  is the unsaturated magnetization.

## 2 Mathematical Framework

The underlying philosophy and assumptions within our approach is that the physics models are 1st order accurate or within 70-80% of the needed accuracy and the error is adequate within the assumed Gaussian noise. Gaussian distributions provide analytical representations of the random variables of interest (ie T1, T2) within the Bayesian setting and provide a crux for understanding. In particular, we say that a random variable  $\eta$  belongs to a multi-variate normal distribution of mean  $\mu \in \mathbb{R}^n$  and covariance  $\Sigma \in \mathbb{R}^{n \times n}$

$$\eta \sim \mathcal{N}(\mu, \Sigma) \Rightarrow p(\eta) = \frac{1}{2 \pi \det \Sigma} \exp \left( -\frac{1}{2} \|\mu - \eta\|_{\Sigma}^2 \right)$$

1. Our data acquisition model,  $\mathcal{G}(\vec{k}, \theta) : \mathbb{R}^a \times \mathbb{R}^m \rightarrow \mathbb{R}^n$ , maps deterministic acquisition parameters,  $\vec{k} \in \mathbb{R}^a$ , and uncertain parameters,  $\theta \in \mathbb{R}^m$  to observables,  $\vec{z} \in \mathbb{R}^n$  ( or  $\vec{z} \in \mathbb{C}^n$ ). Explicitly, we will assume that the measurement models are corrupted by zero mean white noise noise of a **known** covariance matrix,  $\Sigma_z \in \mathbb{R}^{n \times n}$

$$\begin{aligned} \vec{z} &= \mathcal{G}(\vec{k}; \theta) + \eta & \eta &\sim \mathcal{N}(0, \Sigma_z) \\ \vec{k} &= (\text{TE, TR, etc}) \\ \theta &= (\text{T1, T2, etc}) \end{aligned} \tag{1}$$

$\eta$  may be interpreted as the measurement noise or the acquisition noise in the sensor model. For a deterministic measurement model  $\mathcal{G}$ , the conditional probability distribution has an explicit analytical form and may be written as a **known** Gaussian distribution.

$$p(\vec{z}|\theta) = \mathcal{N}(\mathcal{G}(\vec{k}; \theta), \Sigma_z)$$

2. Additional **known** information is the prior probability distributions for the model parameters,  $p(\theta)$ . For simplicity, assume that Prior parameters are Gaussian distributed of **known** mean,  $\hat{\theta}$  and covariance,  $\Sigma_{\theta}$

$$\theta \sim \mathcal{N}(\hat{\theta}, \Sigma_{\theta})$$

3. Bayes theorem is fundamental to the approach. The probability of the measurements  $p(z)$  must be interpreted in terms of the known information. The probability of the measurements may be derived from the marginalization of the joint probability and has the interpretation as the projection of the joint probability onto the measurement axis.

$$p(z) = \int_{\theta} p(\theta, z) d\theta = \int_{\theta} p(z|\theta) p(\theta) d\theta$$

4. The concept of informational entropy [Madankan et al., 2015],  $H(Z)$ , provides a mathematically rigorous framework to look for measurement acquisition parameters,  $\vec{k}$ , with the high information content of the reconstruction. Given a probability space  $(\Omega, \mathcal{F}, p)$  (probability maps from the sigma-algebra of possible events  $p : \mathcal{F} \rightarrow [0, 1]$  sigma-algebra,  $\mathcal{F}$ , defined on set of ‘outcomes’  $\Omega$  [Durrett, 2010]), we will define information of an event as proportional to the inverse probability.

$$\text{information} \equiv \frac{1}{p(z)}$$

Intuitively, when a low probability event occurs this provides high information. The informational entropy is an *average* of the information content for a sigma algebra of events  $\mathcal{F}$

$$H(Z) = \int_Z p(z) \ln \frac{1}{p(z)} dz \quad p(z) = \int_{\theta} p(z|\theta) p(\theta) d\theta$$

Hence this entropy measure is an average of the information content for a given set of events,  $\mathcal{F}$ , and is proportional to the variance or uncertainty in which the set of events occur. This agrees with thermodynamic entropy; if the information containing events are completely spread out such as in a uniform distribution, the entropy is maximized. The entropy is zero for a probability distribution in which only one event occurs. Zero information is gained when the same event always occurs ( $0 \ln \frac{1}{0} = 0$ ). Intuitively, we want to find acquisition parameters,  $\vec{k}$ , for which the measurements are most uncertain

$$\max_k H(Z) \Leftrightarrow \min_k \int_Z dz \underbrace{\int_{\theta} d\theta p(z|\theta) p(\theta)}_{p(z)} \ln \underbrace{\left( \int_{\theta} d\theta p(z|\theta) p(\theta) \right)}_{\ln p(z)}$$

Alternatively we may consider this entropy maximization problem as a sensitivity analysis for the variance of the measurement  $Z$ , ie .  $\max_k H(Z) \approx \max_k \text{Var}(Z)$

$$\begin{aligned} \bar{Z} = \mathbb{E}[Z] &= \int_Z dz z \underbrace{\int_{\theta} d\theta p(z|\theta) p(\theta)}_{p(z)} \\ \mathbb{E}[(Z - \bar{Z})^2] &= \int_Z dz (z - \bar{Z})^2 \underbrace{\int_{\theta} d\theta p(z|\theta) p(\theta)}_{p(z)} \\ &\propto \int_Z dz (z - \bar{z})^2 \int_{\theta} d\theta \exp\left(-\frac{1}{2}\|z - \mathcal{G}(\vec{k}, \theta)\|_{\Sigma_z}^2\right) \exp\left(-\frac{1}{2}\|\theta - \hat{\theta}\|_{\Sigma_{\theta}}^2\right) \end{aligned}$$

Probilistic integrals may be computed from uncertainty quantification techniques [Fahrenholtz et al., 2013].

## References

- [Ahmed and Gokhale, 1989] Ahmed, N. A. and Gokhale, D. (1989). Entropy expressions and their estimators for multivariate distributions. *IEEE Transactions on Information Theory*, 35(3):688–692.
- [Carp et al., 2004] Carp, S. A., Prahl, S. a., and Venugopalan, V. (2004). Radiative transport in the delta-P1 approximation: accuracy of fluence rate and optical penetration depth predictions in turbid semi-infinite media. *Journal of biomedical optics*, 9(3):632–47.
- [Duck, 1990] Duck, F. (1990). Physical properties of tissue: a comprehensive reference book. *London, UK: Academic*.
- [Durrett, 2010] Durrett, R. (2010). *Probability: theory and examples*. Cambridge university press.
- [Fahrenholtz et al., 2015] Fahrenholtz, S., Moon, T., Franco, M., Medina, D., Hazle, J. D., Stafford, R. J., Maier, F., Danish, S., Gowda, A., Shetty, A., Warburton, T., and Fuentes, D. (2015). A Model Evaluation Study for Treatment Planning of Laser Induced Thermal Therapy. *International Journal of Hyperthermia*. in preparation.
- [Fahrenholtz et al., 2013] Fahrenholtz, S., Stafford, R. J., Hazle, J., and Fuentes, D. (2013). Generalised polynomial chaos-based uncertainty quantification for planning MRgLITT procedures. *International Journal of Hyperthermia*, 29(4):324–335. PMC3924420.

- [Fasano et al., 2010] Fasano, A., Hömberg, D., and Naumov, D. (2010). On a mathematical model for laser-induced thermotherapy. *Applied Mathematical Modelling*, 34(12):3831–3840.
- [Fuentes et al., 2013] Fuentes, D., Elliott, A., Weinberg, J. S., Shetty, A., Hazle, J. D., and Stafford, R. J. (2013). An Inverse Problem Approach to Recovery of In-Vivo Nanoparticle Concentrations from Thermal Image Monitoring of MR-Guided Laser Induced Thermal Therapy. *Ann. BME.*, 41(1):100–111. PMC3524364.
- [Fuentes et al., 2010] Fuentes, D., Feng, Y., Elliott, A., Shetty, A., McNichols, R. J., Oden, J. T., and Stafford, R. J. (2010). Adaptive Real-Time Bioheat Transfer Models for Computer Driven MR-guided Laser Induced Thermal Therapy. *IEEE Trans. Biomed. Eng.*, 57(5). Cover Page, PMC3857613.
- [Fuentes et al., 2009] Fuentes, D., Oden, J. T., Diller, K. R., Hazle, J., Elliott, A., , Shetty, A., and Stafford, R. J. (2009). Computational Modeling and Real-Time Control of Patient-Specific Laser Treatment Cancer. *Ann. BME.*, 37(4):763. PMC4064943.
- [Fuentes et al., 2011] Fuentes, D., Walker, C., Elliott, A., Shetty, A., Hazle, J., and Stafford, R. J. (2011). MR Temperature Imaging Validation of a Bioheat Transfer Model for LITT. *International Journal of Hyperthermia*, 27(5):453–464. Cover Page, PMC3930085.
- [MacLellan et al., 2013] MacLellan, C. J., Fuentes, D., Elliott, A. M., Schwartz, J., Hazle, J. D., and Stafford, R. J. (2013). Estimating nanoparticle optical absorption with magnetic resonance temperature imaging and bioheat transfer simulation. *International Journal of Hyperthermia*, (0):1–9.
- [Madankan et al., 2015] Madankan, R., Stefan, W., Hazle, J. D., Stafford, R. J., and Fuentes, D. (2015). Accelerated Model-based Signal Reconstruction for Magnetic Resonance Imaging in Presence of Uncertainties. *IEEE Trans. Med. Img.* submitted.
- [Martin et al., 2012] Martin, J., Wilcox, L. C., Burstedde, C., and Ghattas, O. (2012). A stochastic newton mcmc method for large-scale statistical inverse problems with application to seismic inversion. *SIAM Journal on Scientific Computing*, 34(3):A1460–A1487.
- [Modest, 2013] Modest, M. F. (2013). *Radiative heat transfer*. Academic press.
- [Needles et al., 2010] Needles, A., Heinmiller, A., Ephrat, P., Bilan-Tracey, C., Trujillo, A., Theodoropoulos, C., Hirs-son, D., and Foster, F. (2010). Development of a combined photoacoustic micro-ultrasound system for estimating blood oxygenation. In *Ultrasonics Symposium (IUS), 2010 IEEE*, pages 390–393. IEEE.
- [Stefan et al., 2015] Stefan, W., Fuentes, D., Yeniaras, E., Hwang, K., Hazle, J. D., and Stafford, R. J. (2015). Novel Method for Background Phase Removal on MRI Proton Resonance Frequency Measurements. *Trans. Medical Imaging*. in review.
- [Welch, 1984] Welch, A. J. (1984). The thermal response of laser irradiated tissue. *Quantum Electronics, IEEE Journal of*, 20(12):1471–1481.
- [Welch and Van Gemert, 1995] Welch, A. J. and Van Gemert, M. J. (1995). *Optical-thermal response of laser-irradiated tissue*, volume 1. Springer.
- [Wray et al., 1988] Wray, S., Cope, M., Delpy, D. T., Wyatt, J. S., and Reynolds, E. O. R. (1988). Characterization of the near infrared absorption spectra of cytochrome aa3 and haemoglobin for the non-invasive monitoring of cerebral oxygenation. *Biochimica et Biophysica Acta (BBA)-Bioenergetics*, 933(1):184–192.
- [Yung et al., 2015] Yung, J., Fuentes, D., MacLellan, C. J., Maier, F., Hazle, J. D., and Stafford, R. J. (2015). Referenceless Magnetic Resonance Temperature Imaging using Gaussian Process Modeling. *Medical Physics*. in review.