# Lorentzian Fitting of the CEST Z-Spectra in Blood Red Cells

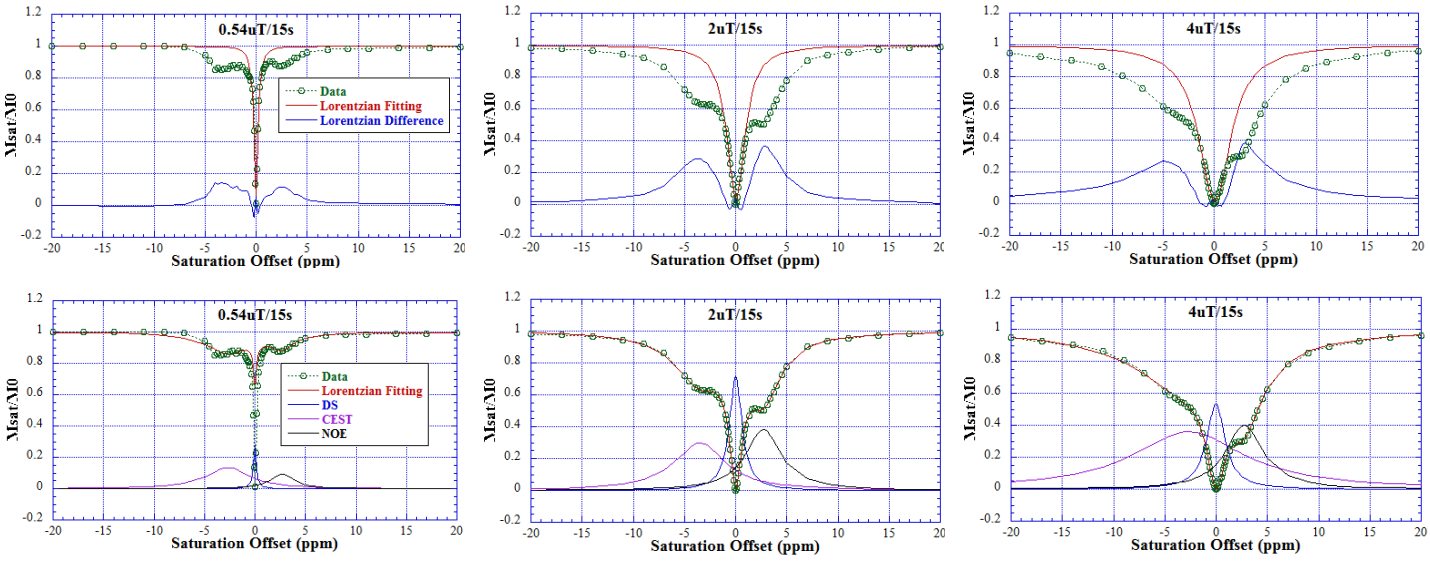
Shaokuan Zheng[1], Guoxing Lin[2], Zhongliang Zu[3], Yansong Zhao[4], and Matthew J Gounis[1]

[1]*Department of Radiology, UMASS Medical School, Worcester, MA, United States,* [2]*Gustav H. Carlson School of Chemistry, Clark University, Worcester, MA, United States,* [3]*Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States,* [4]*Philips Healthcare, Cleveland, OH, United States*

**Target audience:** Researchers and physicians who are interested in the biophysical and biochemical mechanism of blood Chemical Exchange Saturation Transfer (CEST) effect.

**Purpose**: CEST MRI is a new imaging technique which can be used to detect the signal from proteins and peptides by saturating the exchangeable labile protons of amide protons (-NH), amine protons (-$NH_2$) and hydroxyl protons (-OH)[1]. It has been proven that blood is a suitable CEST agent for generating sufficient CEST contrast vs. surrounding tissue[2]. Since regional blood perfusion and changes in vascular permeability are important characteristics of various diseases, e.g. cancer and stroke, the understanding of CEST properties of blood would potentially benefit various applications of CEST in diagnosis and staging of various pathologies. CEST imaging in tissue is very complex as it in general includes Nuclear Overhauser Enhancement (NOE) effect; and it is not only depends on tissue properties (labile proton concentration, proton exchange rate, T1 and T2 value), but also on experimental parameters (magnetic field strength, saturation scheme). To have more insight into how contrast can be achieved in CEST/NOE imaging in tissue, it is required to know the dynamic properties of the active CEST/NOE agent(s) present in the tissue. So far, most studies on the measurement of chemical exchange rate are limited to simple phantoms with one CEST active site[3] or PARACEST agents[4] because it is hard to separate CEST and NOE effect in tissue accurately. Currently, there are two analysis methods to get pure CEST and NOE effect. The first method is to fit the data, which is acquired by using low-power long-duration saturation pulse, by using Lorentzian difference (LD) analysis[5]. In this case, only those data acquired near to water frequency and far away from CEST/NOE frequency were used to remove the direct saturation (DS) effect, this method is referred to as Lorentzian fitting I in this abstract. The second method assumes that the Z-spectra are a superposion of multiple Lorentzian lines and all data are used for fitting[6]. This method is named Lorentzian fitting II here. Herein, we evaluate how these two Lorentzian fitting methods work at different saturation powers. Three typical saturation powers of 0.54 uT, 2 uT and 4 uT were used to represent low, medium and high power level.

**Methods**: Arterial blood samples were collected from pigs which were used for an unrelated study. Whole blood samples were mixed (ratio 10:1) with Anticoagulant Citrate Dextrose (ACD) solution (Baxter healthcare Cor. North Carolina 28752) immediately after collection. Whole blood sample was centrifuged (Centrifuge 5804R, Eppendorf AG, Hamburg, Germany) with 2000 rcf for 10 minutes to separate plasma from red blood cells and platelets. Red blood cells were placed in standard 5 mm NMR tubes for NMR spectroscopy. All 1H NMR Z-spectrum experiments were performed on a 14.1 T Varian Unity Inova spectrometer equipped with a 5-mm triple resonance probe. Spectroscopy data was acquired from red blood cells at room temperature. A flip angle of 10 degrees was used to decrease the radiation damping effect. The Z-spectra were acquired with pre-saturation duration of 15 seconds, powers of 0.54 $\mu T$, 2 $\mu T$, 4 $\mu T$, and 61 off-resonance uneven steps from 40 ppm to -40 ppm. One more spectrum was acquired at an offset of 500 ppm for signal normalization for each Z-spectrum. The Z-spectra were used for Lorentzian analysis with a linear baseline drift correction. For the Lorentzian fitting method I, three regions of Z-spectra (|f|<1pp and |f|>10ppm) were used. The repetition time used was 20 seconds and a line broadening of 1 Hz was used for Fourier transformation.




**Results and Discussion**: The Z-spectra of red cells at different power saturations are shown in the above figures. The figures in the upper row are the results by using the Lorentzian fitting method I, red and blue lines are the Lorentzian fitting curve and the Lorentzian difference analysis results, respectively. The figures in the bottom row are the results by using the Lorentzian fitting method II, red, blue, purple and black lines are the Lorentzian fitting curve, direction saturation (DS) component, CEST component and NOE component, respectively. From these figures, we can see that Lorentzian fitting method I has a good fitting for Z-spectra acquired at low saturation power and Lorentzian fitting method II has a good fitting for Z-spectra acquired at both medium and high saturation power.

**References**: [1] Zhou JY *et al. Prog Nucl Mag Res*. 2006;48:109-136. [2] Zheng SK *et al. Magn Reson Med*. 2014; 71: 1082-1092. [3] Sun ZP *et al. Contrast Medium Mol. Imaging* 2014; 9: 268-275. [4] Dixon TW et al. *Magn Reson Med*. 2010; 63: 625-632. [5] Jones C *et al*, *NeuroImage* 2013;77:114-124.[6] Zaiss MW *et al. Proc. Intl. Soc. Mag. Reson. Med.* 18 (2010): 5136.