In Vivo GABA/Glx Detection and Quantification for Small Animals.
–- MEGA-PRESS Sequence

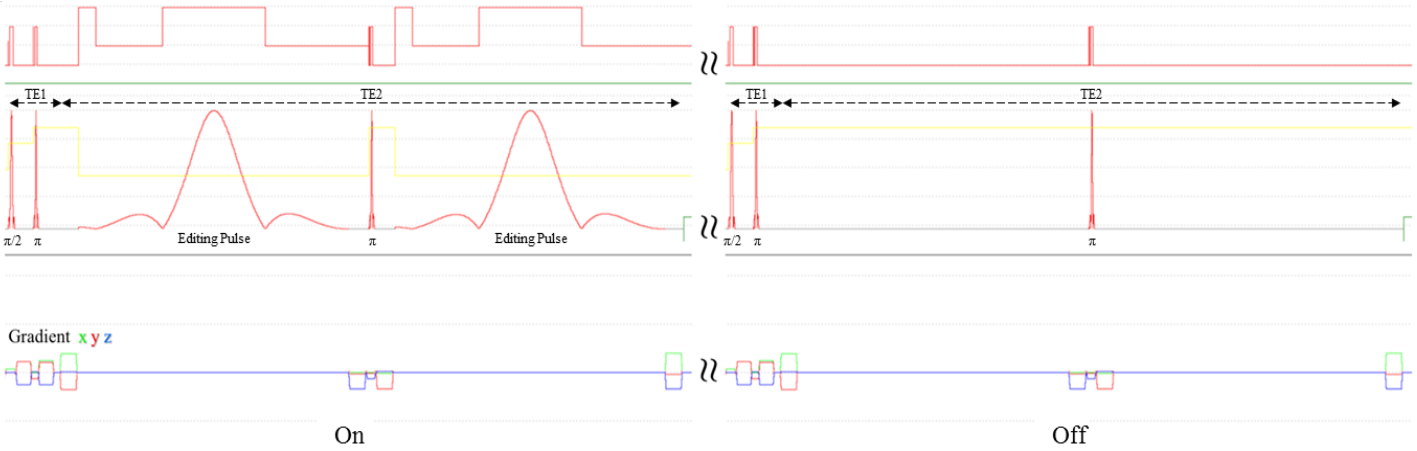


FIGURE 1: Representative MEGA-PRESS pulse sequence (with TE1=5 ms and TE2=67 ms), showing the addition of the editing pulses symmetrically around the sec 180^{o} pulse in the 'On' mode comparing to the standard PRESS sequence used in the 'Off' mode.

In Vivo GABA/Glx Detection and Quantification for Small Animals.
–- Phantom Test

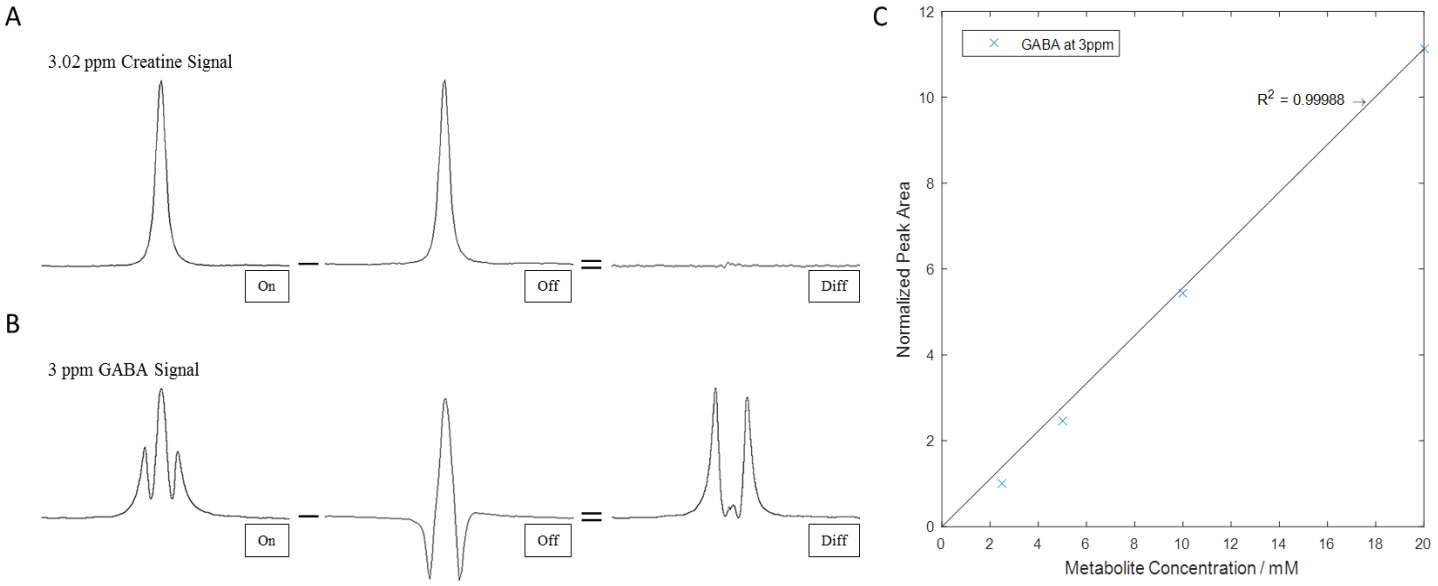


FIGURE 2: In vitro results of MEGA-PRESS editing for GABA solutions. Editing pulses applied at 1.9 ppm modulate the GABA singles at 3 ppm. (A) The effect of editing pulses on creatine signal at 3.02 ppm; perfect cancelation of creatine signal was observed in the difference spectrum (labeled Diff) using 20mM creatine solution by subtracting scans acquired without editing pulses (Off) from scans acquired with editing pulses (On). (B) The effect of editing pulses on GABA signal at 3 ppm; theoretical 'pseudo-doublet' shape of edited GABA signal was observed in the difference spectrum using 20mM GABA solution. (C) Normalized GABA peak areas at 3 ppm (normalized by the result of 2.5mM GABA solution) have good agreement (R2>0.999) with prepared GABA solution concentrations (i.e., 2.5 mM, 5 mM, 10 mM and 20mM).

In Vivo GABA/Glx Detection and Quantification for Small Animals.
–- In Vivo Test

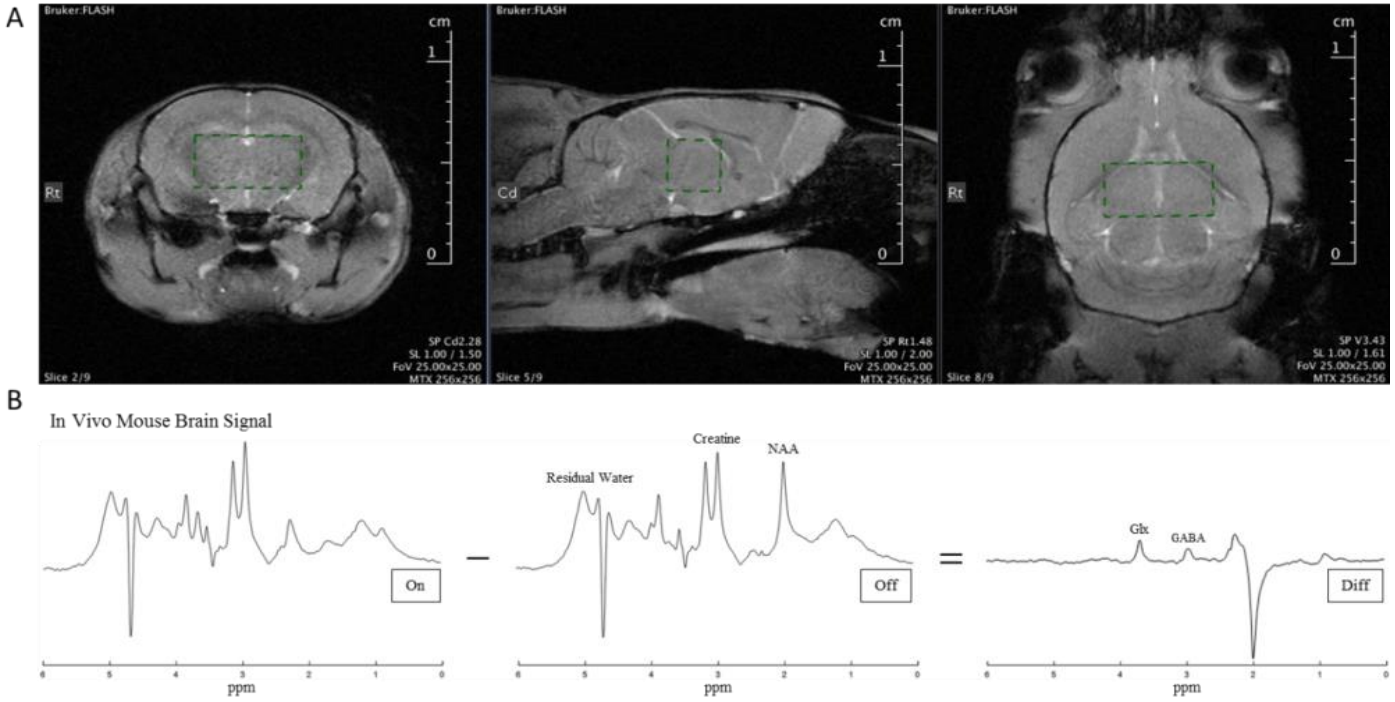
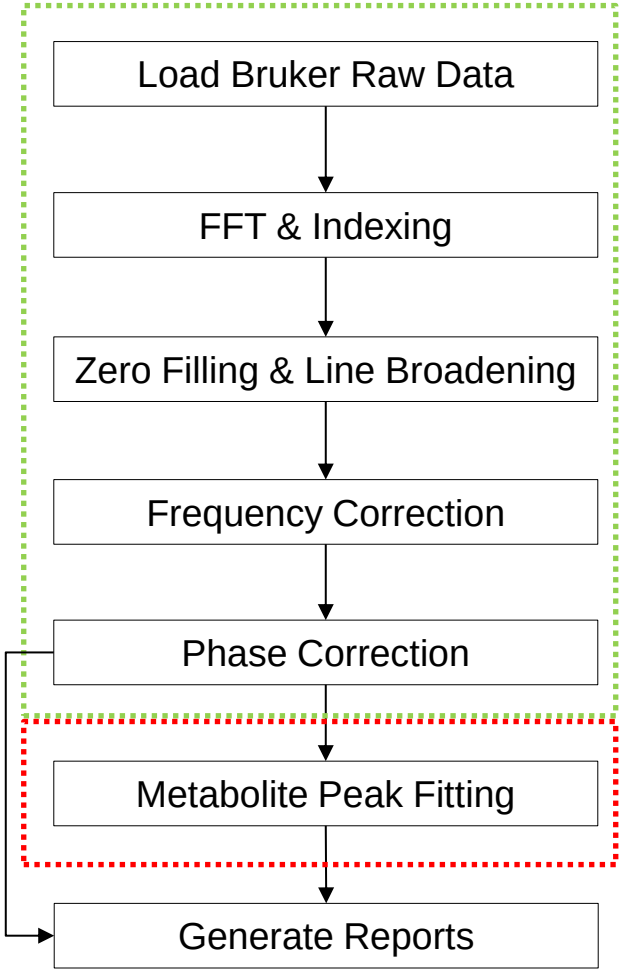


FIGURE 3: (A) Bruker Paravision 6.0.1 screenshot showing the voxel placement at the mouse thalamus for MEGA-PRESS acquisition. The voxel position was determined based up T1-weighted anatomical scans with voxel dimensions: 5 mm (RL) × 3 mm (AP) × 3 mm (SI) as shown. (B) Representative diagram of MEGA-PRESS editing from one subject, removal of overlying creatine signals from the edited spectrum reveals the GABA signal in the difference spectrum (Diff) by subtracting scans acquired without editing pulses (Off) from scans acquired with editing pulses (On). All spectra were generated from Mouse-Gannet with line broadening of 14 Hz.

In Vivo GABA/Glx Detection and Quantification for Small Animals.
–- Mouse-Gannet Framework

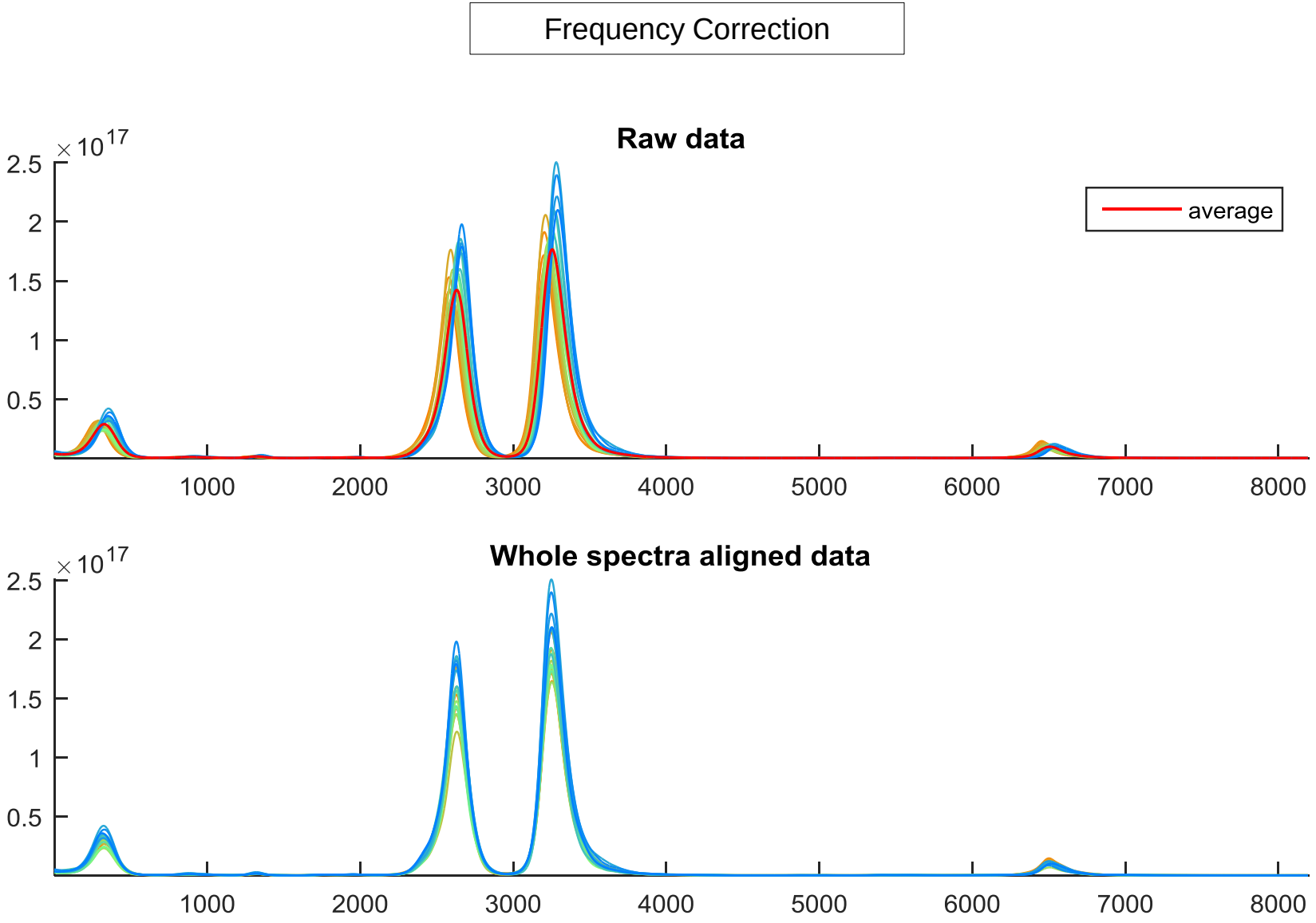
Mouse-Gannet Automated Framework



Loading Module

Fitting Module

In Vivo GABA/Glx Detection and Quantification for Small Animals. –- Mouse-Gannet Framework >> Loading Module >> Frequency Correction



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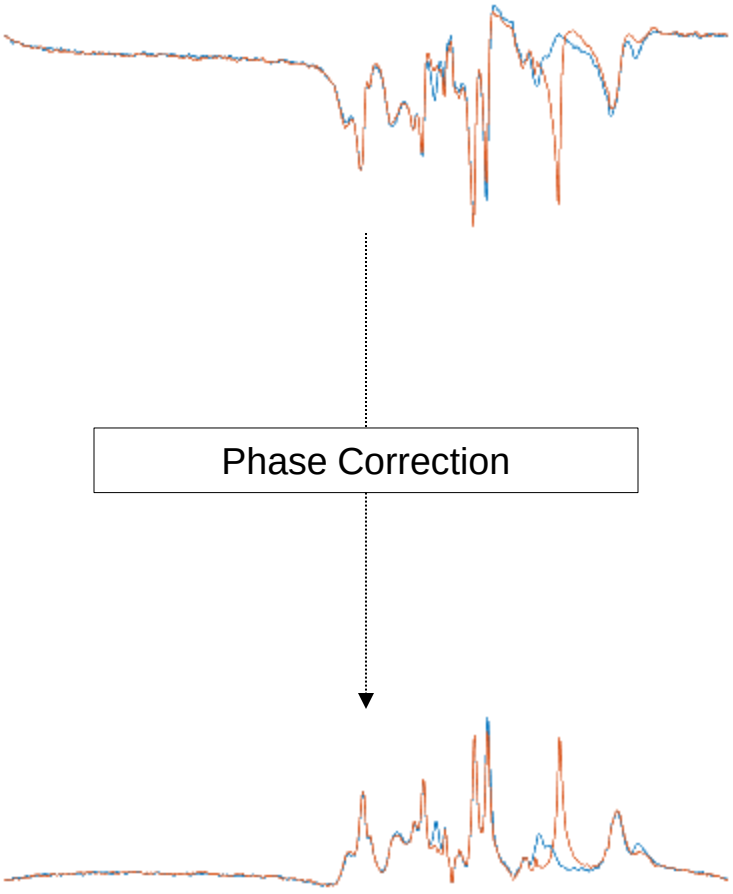
In Vivo GABA/Glx Detection and Quantification for Small Animals. –- Mouse-Gannet Framework >> Loading Module >> Phase Correction



$$R_i = R_i^0 \cos(\phi_i) - I_i^0 \sin(\phi_i),$$

$$I_i = I_i^0 \cos(\phi_i) + R_i^0 \sin(\phi_i),$$

$$\phi_i = phc0 + phc1 \times \frac{i}{n},$$

$$\text{Min}\, E = -\sum_i h_i \ln h_i + P(R_i)$$

w.r.t. $phc0, phc1$

$$h_i = \frac{|R_i^m|}{\sum_i |R_i^m|}$$

$$R_i = R_i^0 \cos(\phi_i) - I_i^0 \sin(\phi_i)$$

$$\phi_i = phc0 + phc1 \times \frac{i}{n}.$$

$$P(R_i) = \gamma \left[\sum_i F(R_i) R_i^2 \right],$$

$$F(y) = \begin{cases} 0, & y \geqslant 0 \\ 1, & y < 0. \end{cases}$$

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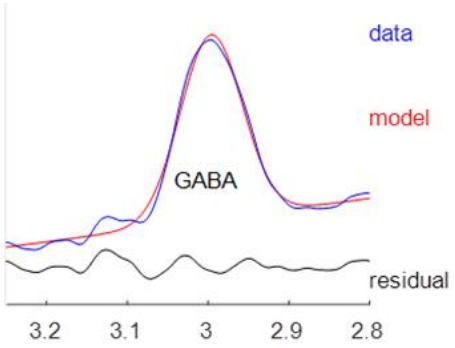
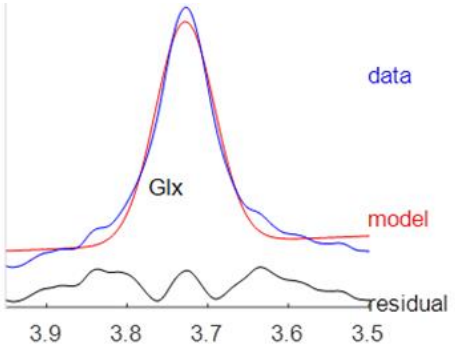
In Vivo GABA/Glx Detection and Quantification for Small Animals. –- Mouse-Gannet Framework >> Fitting Module

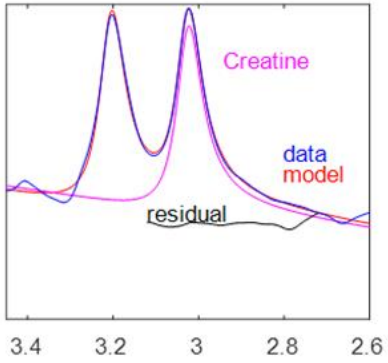


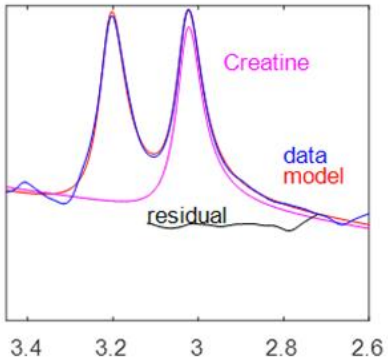
filename : .\166\rawdata.job0
320 averages of a 0.045 ml voxel
GABA+ Area : 56.5
Cr Area : 923.0902
FitError (GABA&Cr): 3.79%
GABA+/Cr i.r.: 0.0612

C



filename : .\166\rawdata.job0
320 averages of a 0.045 ml voxel
Glx Area : 81.1
Cr Area : 923.0902
FitError (Glx&Cr): 4.87%
Glx+/Cr i.r.: 0.0878





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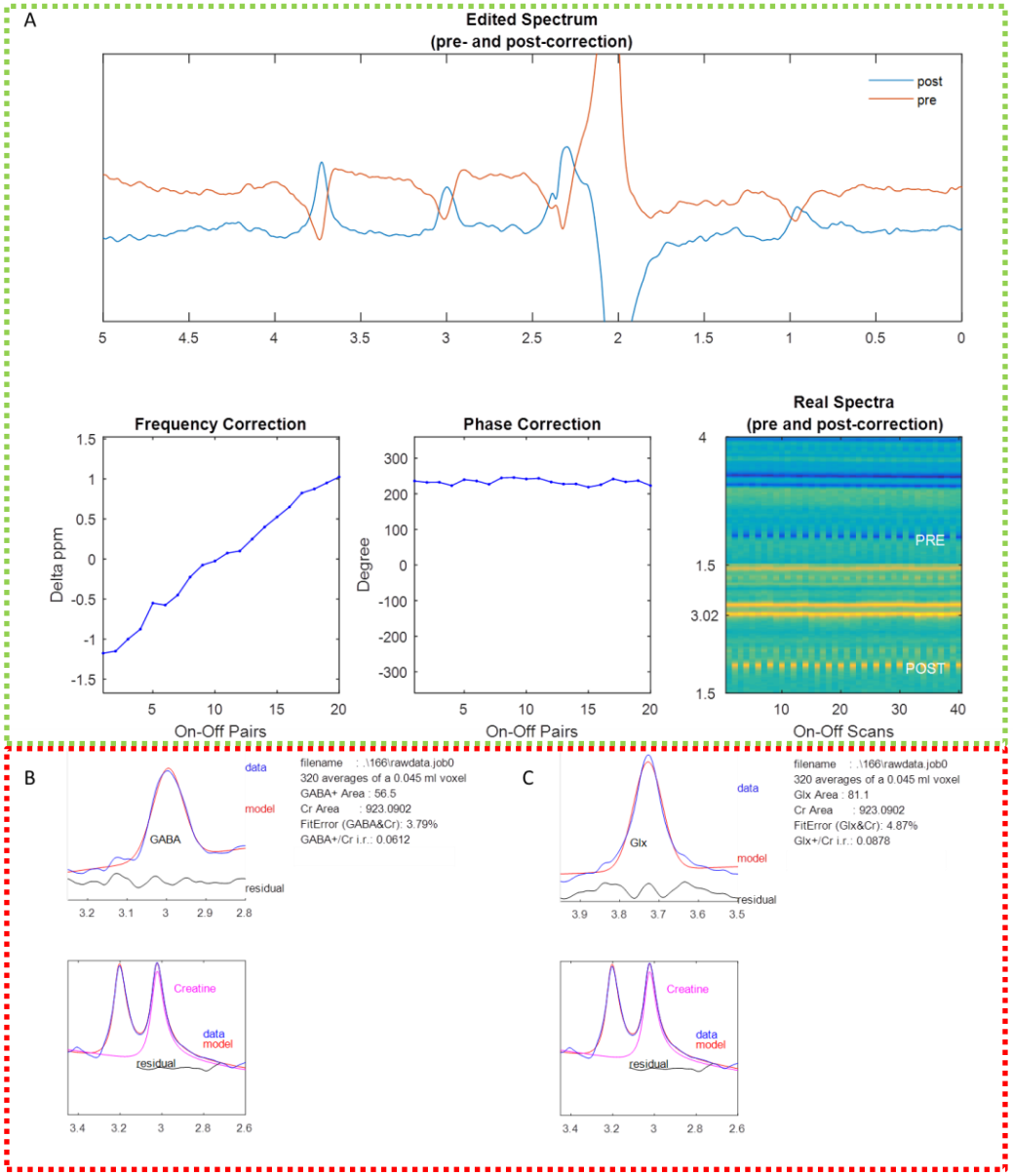
In Vivo GABA/Glx Detection and Quantification for Small Animals.

–- Mouse-Gannet Framework >> Software Reports

Mouse-Gannet output reports.



Loading Module

Fitting Module

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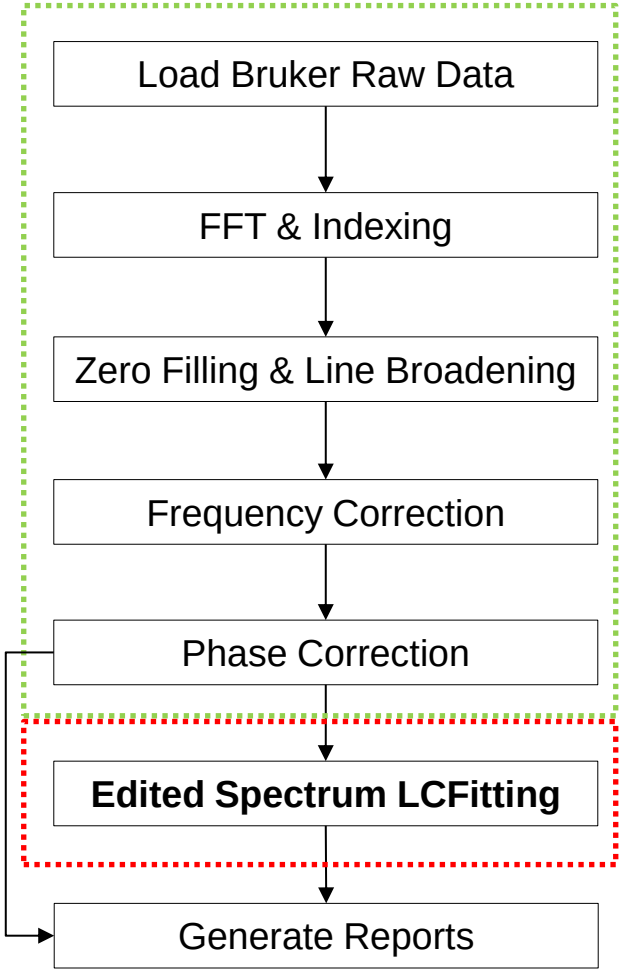
In Vivo GABA/Glx Detection and Quantification for Small Animals.
–- A New Framework

Mouse MEGA-PRESS Spectrum Quantification Toolkit with Simulated Metabolite Basis Set
"Mouse-SpecQuanT"

Jia, 10/10/2016

Mouse-SpecQuanT
– Framework Pipeline

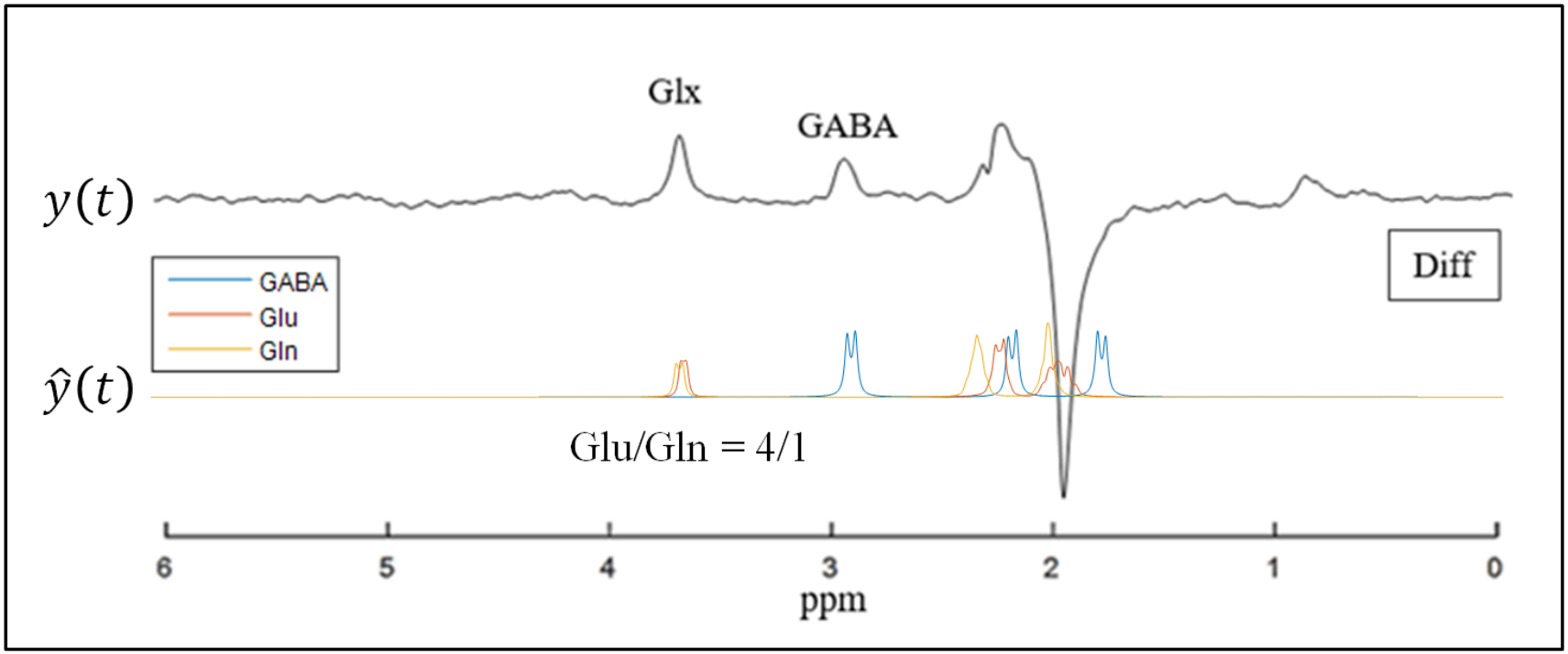
Mouse-SpecQuanT Automated Framework



Loading Module

Fitting Module

Mouse-SpecQuanT
– Fitting Model



$$Model \qquad y(t) = \hat{y}(t) + \epsilon_t \,, t = t_0, \ldots, t_{M-1}$$

$$Estimation \qquad \hat{y}(t) = \sum_{k=1}^{K} a_k \zeta_k(\gamma_k, t) v_k(t)$$

Mouse-SpecQuanT
– Fitting Model

$$Model \qquad y(t) = \hat{y}(t) + \epsilon_t \,, t = t_0, \dots, t_{M-1}$$

$$Estimation \qquad \hat{y}(t) = \sum_{k=1}^{K} a_k \zeta_k(\gamma_k, t) v_k(t)$$

$where$ a_k --- weighting coefficients

$v_k(t)$ −−− simulated individual metabolite FID (i.e., GABA, Glx)

$$\zeta_k(\gamma_k, t) = 1\exp(-R_k t)\, \exp\big(i(\Omega_k t + \phi_k)\big)$$

$$\gamma_k = \{R_k, \Omega_k, \phi_k\}$$

$$then \quad \{\boldsymbol{a}, \boldsymbol{\gamma}\} = argmin(\left\|\boldsymbol{Y} - \widehat{\boldsymbol{Y}}\right\|^2)$$

$finally$ a_k

$\{R_k, \Omega_k, \phi_k\} \leftarrow \gamma_k$

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Mouse-SpecQuanT
– Fitting Model

$$\widehat{\boldsymbol{Y}} = \begin{bmatrix} \zeta_1(\gamma_1, t_0)v_1(t_0) & \cdots & \zeta_K(\gamma_K, t_0)v_k(t_0) \\ \vdots & \ddots & \vdots \\ \zeta_1(\gamma_1, t_{M-1})v_1(t_{M-1}) & \cdots & \zeta_K(\gamma_K, t_{M-1})v_K(t_{M-1}) \end{bmatrix} \begin{bmatrix} a_1 \\ \vdots \\ a_K \end{bmatrix} = \boldsymbol{\Phi a}$$

$$where \quad \{\boldsymbol{a}, \boldsymbol{\gamma}\} = argmin(\|\boldsymbol{Y} - \boldsymbol{\Phi a}\|^2)$$

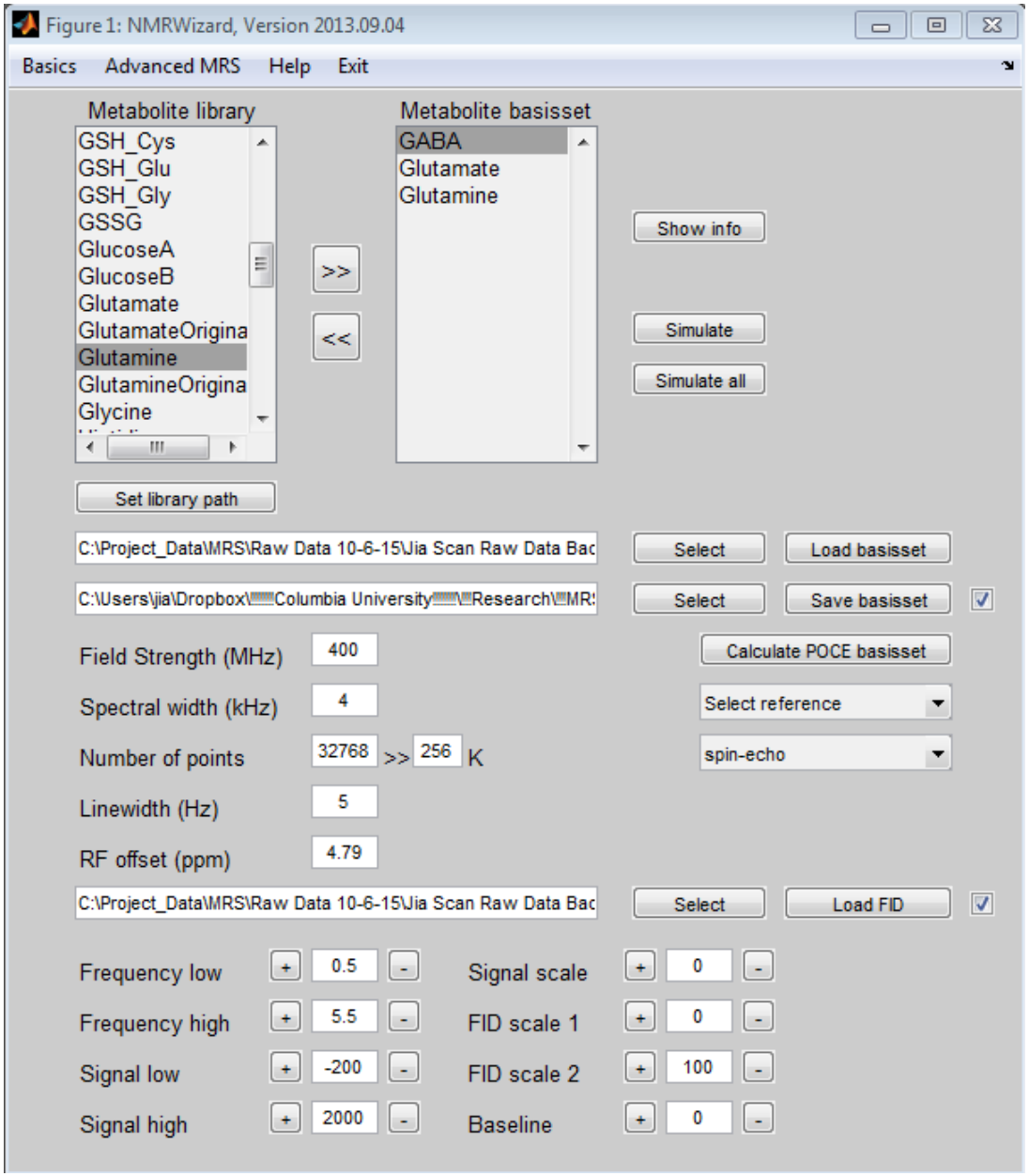
$$then \quad \boldsymbol{\gamma^{nlls}} = \underset{\boldsymbol{\gamma}}{argmin}(\|(\boldsymbol{I} - \boldsymbol{\Phi\Phi}^+)\boldsymbol{Y}\|^2)$$

$$\boldsymbol{a^{ls}} = \boldsymbol{\Phi}^+(\boldsymbol{\gamma^{nlls}})\boldsymbol{Y}$$

$$finally \quad a_k$$

$$\{R_k, \Omega_k, \phi_k\} \leftarrow \gamma_k$$

Mouse-SpecQuanT
– Basis Set Simulation with 'NMRWizard' (by Graff Robin at Yale)



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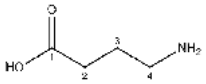
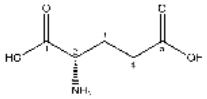
Mouse-SpecQuanT
– Basis Set Simulation with 'NMRWizard' (by Graff Robin at Yale)

GABA

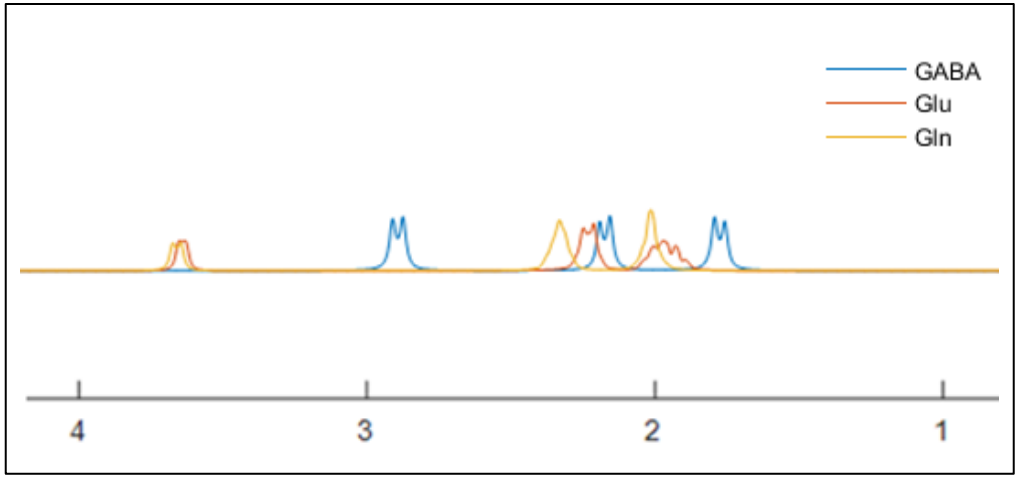


Proton	CS(ppm)	Interaction	J(Hz)
H2	2.2872	J22	0
H2'	2.2872	J23	7.3
H3	1.8919	J23'	7.3
H3'	1.8919	J24	0
H4	3.003	J24'	0
H4'	3.003	J2'3	7.3
		J2'3'	7.3
		J2'4	0
		J2'4'	0
		J33'	0
		J34	7.3
		J34'	7.3
		J3'4	7.3
		J3'4'	7.3
		J44'	0

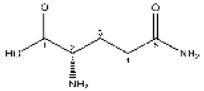
Glutamate



Proton	CS(ppm)	Interaction	J(Hz)
H2	3.7481	J23	4.65
H3	2.1197	J23'	7.33
H3'	2.046	J24	0
H4	2.3521	J24'	0
H4'	2.3342	J33'	-14.76
		J34	6.73
		J34'	8.77
		J3'4	8.7
		J3'4'	6.28
		J44'	-16.03



Glutamine



Proton	CS(ppm)	Interaction	J(Hz)
H2	3.767	J23	5.91
H3	2.1365	J23'	6.71
H3'	2.1207	J24	0
H4	2.4575	J24'	0
H4'	2.4312	J33'	-14.45
		J34	6.32
		J34'	9.34
		J3'4	9.4
		J3'4'	6.18
		J44'	-15.61

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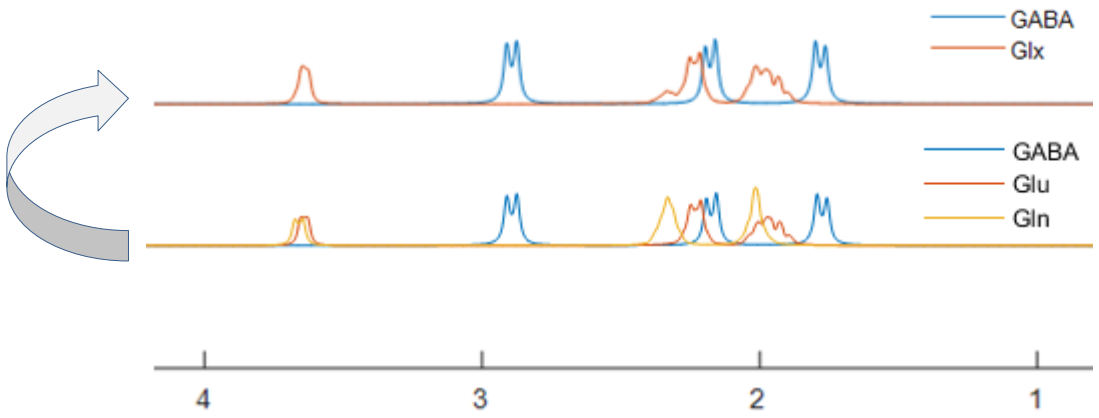
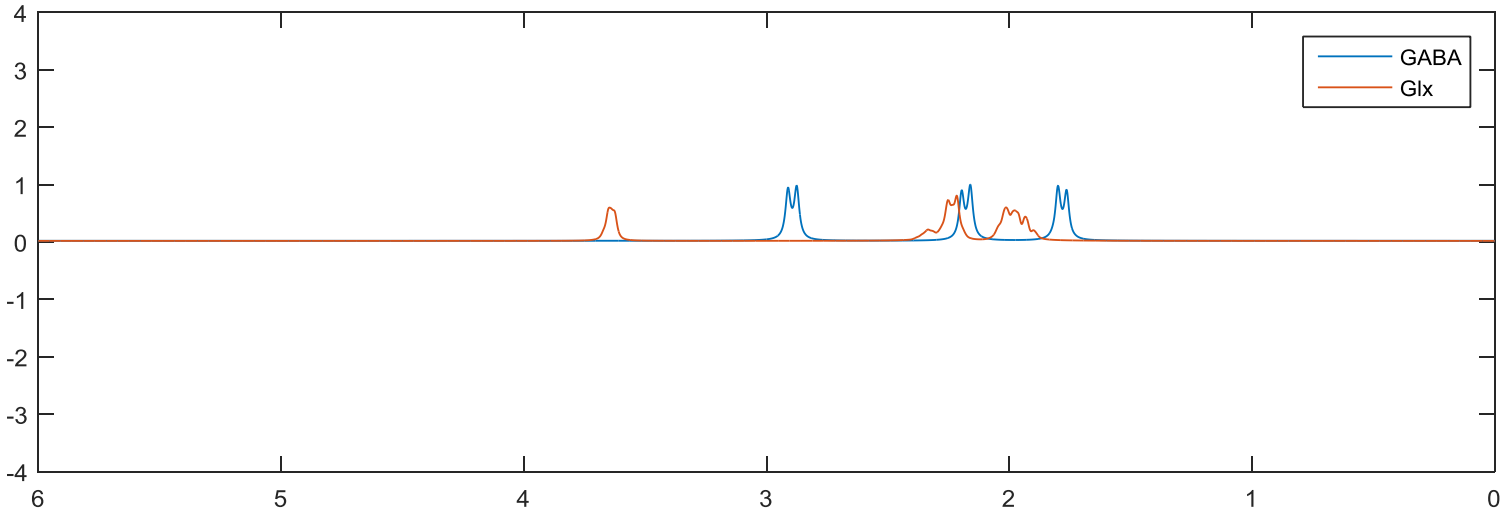
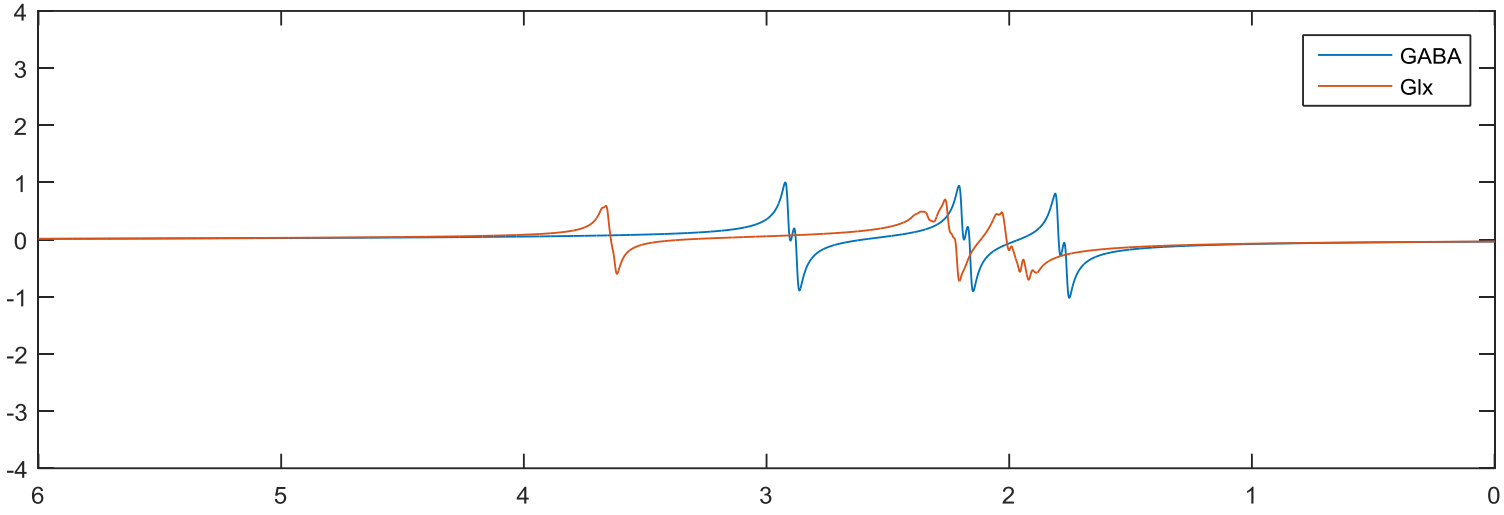
Mouse-SpecQuanT
– Basis Set Simulation with ‘NMRWizard’ (by Graff Robin at Yale)

Glx = 0.8*Glu + 0.2*Gln



Mouse-SpecQuanT
– Simulated Basis Set





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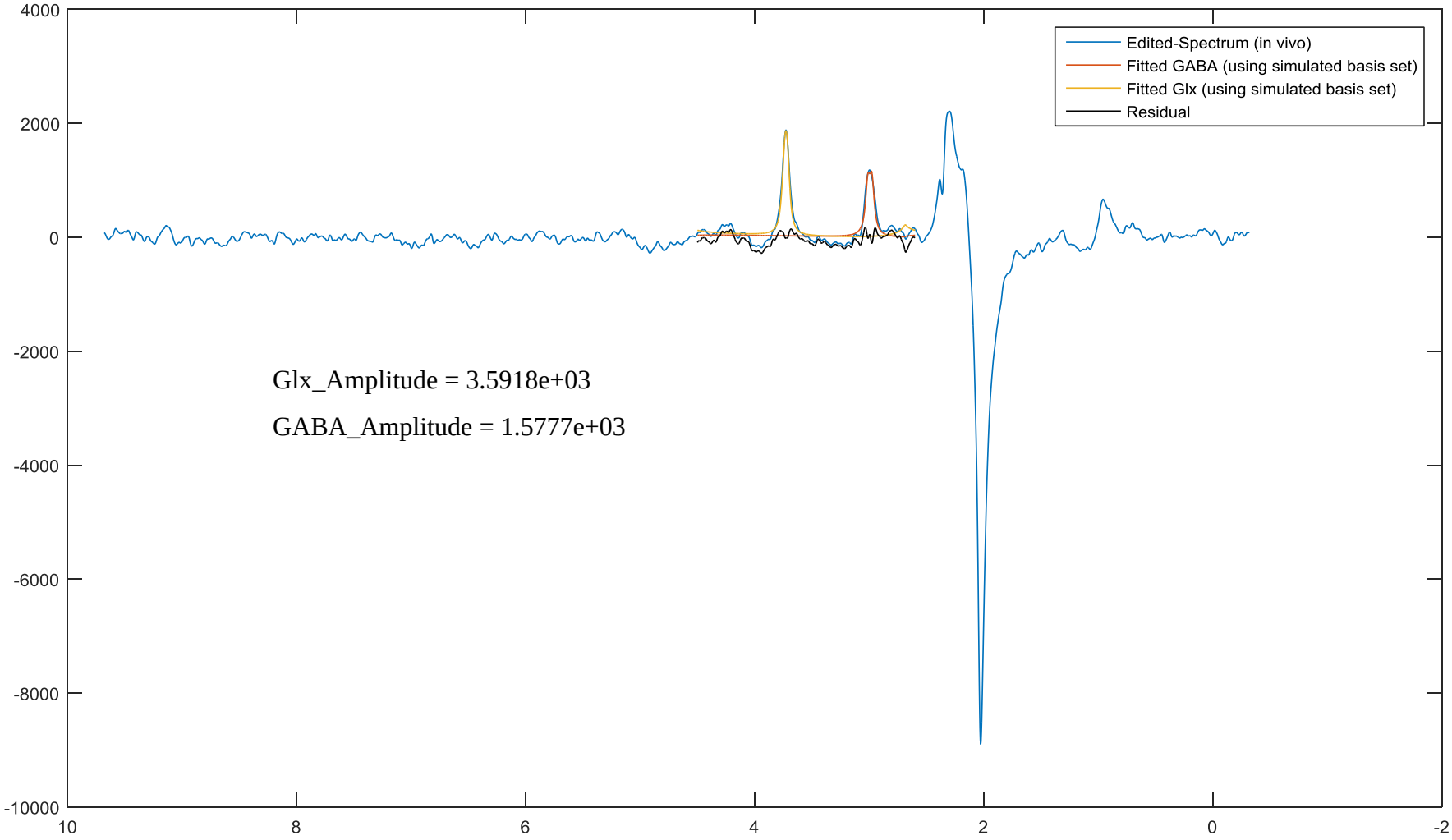
Mouse-SpecQuanT
– Fitting Result with Lorentzian Lineshape



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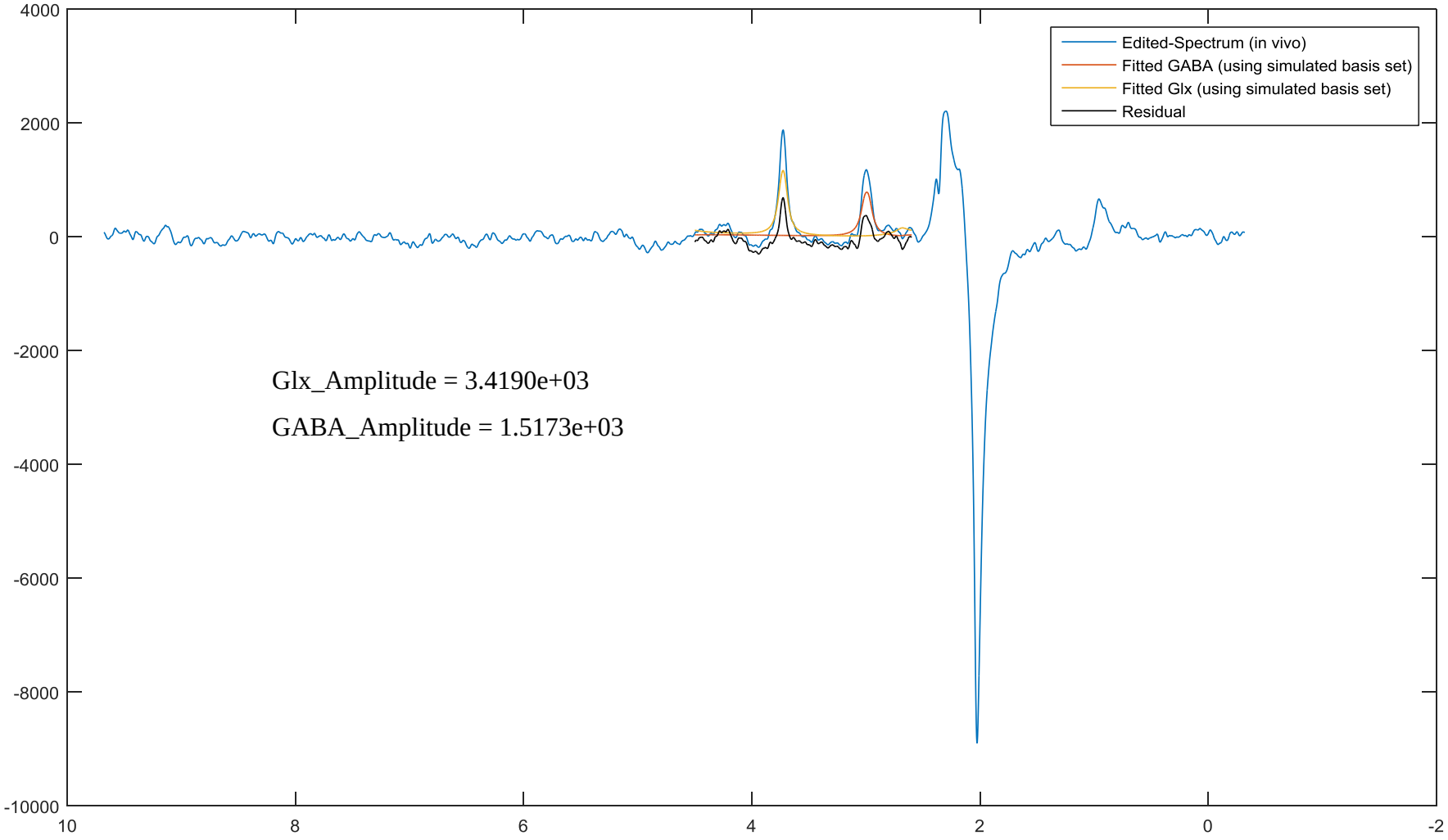
Mouse-SpecQuanT
– Fitting Result with Gaussian Lineshape



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Mouse-SpecQuanT
– Fitting Function Source Code

```
function FitSpec=SQSBS(x, time, FID_basis, LB_mode) % spectrum quantification with simulated basis set

% Jia, 10/10/16
% Please contact jg3400@columbia.edu if you have questions.

GABA_Amplitude = x(1,1);
GABA_LB = x(1,2);
GABA_ChemShift = x(1,3);

Glx_Amplitude = x(2,1);
Glx_LB = x(2,2);
Glx_ChemShift = x(2,3);

switch LB_mode
    case 1 % Lorenzian Line Broadening
        FitFID = GABA_Amplitude.*FID_basis(1,:).*exp(-GABA_LB.*time*pi).*exp(1i.*time.*GABA_ChemShift.*400.*6.28)+...
            Glx_Amplitude.*FID_basis(2,:).*exp(-Glx_LB.*time*pi).*exp(1i.*time.*Glx_ChemShift.*400.*6.28);
    case 2 % Gaussian Line Broadening
        FitFID = GABA_Amplitude.*FID_basis(1,:).*exp(-GABA_LB^2.*time.^2*pi).*exp(1i.*time.*GABA_ChemShift.*400.*6.28)+...
            Glx_Amplitude.*FID_basis(2,:).*exp(-Glx_LB^2.*time.^2*pi).*exp(1i.*time.*Glx_ChemShift.*400.*6.28);
end
FitSpec = real(fft(FitFID));
```