

Supplementary Materials

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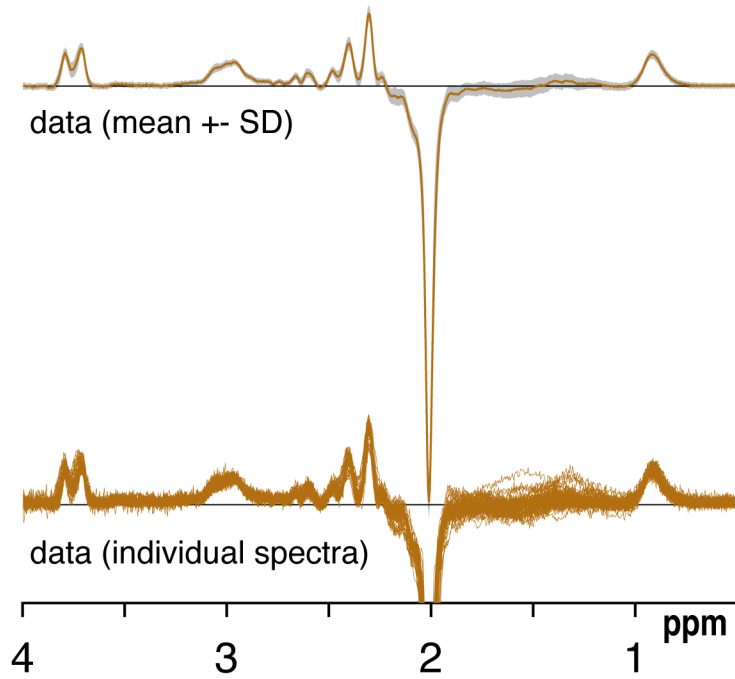
Supplementary Material 1 – List of included subjects. All datasets are available at <https://www.nitrc.org/projects/biggabe/>

| site | subjects | Σ |
|--------------------------------|---|---------------------------------|
| P01 | S01,S03,S04,S05,S08 | 5 |
| P03 | S02,S03,S04,S07,S08,S09,S10,S11,S12 | 9 |
| P05 | S01,S02,S03,S05,S06,S07,S08 | 7 |
| P06 | S01,S02,S03,S04,S05,S06,S07,S08,S09 | 9 |
| P07 | S02,S03,S04,S09,S10,S11,S12 | 7 |
| P08 | S01,S02,S03,S04,S05,S06,S07,S08,S09,S10,S11,S12 | 12 |
| P09 | S01,S02,S03,S04,S05,S06,S07,S08,S09,S10,S11,S12 | 12 |
| $\Sigma = 7$ | | $\Sigma = 61$ |

Supplementary Material 2. Properties of the Gaussian functions of the broad macromolecule and lipid resonances included in the basis sets, taken from section 11.7 of the LCModel manual. The amplitude values are scaled relative to the CH₃ singlet of creatine with amplitude 3.

| <i>Name</i> | <i>Frequencies [ppm]</i> | <i>FWHM [ppm]</i> | <i>Amplitude</i> |
|--------------------------------------|--------------------------|-------------------|------------------|
| <i>edit-OFF spectrum basis set</i> | | | |
| MM _{0.94} | 0.915 | 0.14 | 3.00 |
| MM _{1.22} | 1.22 | 0.15 | 2.00 |
| MM _{1.43} | 1.43 | 0.17 | 2.00 |
| MM _{1.70} | 1.67 | 0.15 | 0.20 |
| MM _{2.05} | 2.08 | 0.15 | 1.33 |
| | 2.25 | 0.20 | 0.33 |
| | 1.95 | 0.15 | 0.33 |
| | 3.00 | 0.20 | 0.40 |
| Lip09 | 0.89 | 0.14 | 3.00 |
| Lip13 | 1.28 | 0.15 | 2.00 |
| | 1.28 | 0.089 | 2.00 |
| Lip20 | 2.04 | 0.15 | 1.33 |
| | 2.25 | 0.15 | 0.67 |
| | 2.80 | 0.20 | 0.87 |
| <i>Difference spectrum basis set</i> | | | |
| MM _{0.94} | 0.915 | 0.14 | 3 |
| MM _{3co} | 3 | 14 Hz | 2 |

Data overview



Supplementary Material 3 – Overview of the processed data including the mean \pm SD and individual data.

Supplementary Material 4 – GABA mean and SDs for all modeling strategies (ratios to tCr). Significant differences ($p < .05$) between the corresponding model and the 'none' model (gray shade) are indicated in bold.

| modeling range | | narrow | | | intermediate | | | wide | | |
|------------------------------|--------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| knot spacing (ppm) | | 0.55 | 0.4 | 0.25 | 0.55 | 0.4 | 0.25 | 0.55 | 0.4 | 0.25 |
| none | [GABA] | 0.220 | 0.213 | 0.193 | 0.297 | 0.186 | 0.204 | 0.284 | 0.288 | 0.158 |
| | | <i>.062</i> | <i>.071</i> | <i>.057</i> | <i>.048</i> | <i>.061</i> | <i>.044</i> | <i>.029</i> | <i>.034</i> | <i>.066</i> |
| GABA_{hard} | [GABA] | 0.164 | 0.146 | 0.156 | 0.207 | 0.148 | 0.165 | 0.194 | 0.207 | 0.150 |
| | | <i>.021</i> | <i>.02</i> | <i>.023</i> | <i>.024</i> | <i>.031</i> | <i>.021</i> | <i>.021</i> | <i>.023</i> | <i>.034</i> |
| GABA_{soft} | [GABA] | 0.108 | 0.102 | 0.108 | 0.207 | 0.130 | 0.148 | 0.203 | 0.204 | 0.115 |
| | | <i>.024</i> | <i>.027</i> | <i>.025</i> | <i>.048</i> | <i>.039</i> | <i>.03</i> | <i>.026</i> | <i>.027</i> | <i>.049</i> |
| Gauss_{fixed} | [GABA] | 0.074 | 0.080 | 0.081 | 0.174 | 0.106 | 0.118 | 0.136 | 0.145 | 0.108 |
| | | <i>.031</i> | <i>.031</i> | <i>.035</i> | <i>.055</i> | <i>.045</i> | <i>.045</i> | <i>.031</i> | <i>.032</i> | <i>.068</i> |
| Gauss_{free} | [GABA] | 0.079 | 0.078 | 0.081 | 0.180 | 0.107 | 0.119 | 0.137 | 0.145 | 0.107 |
| | | <i>.034</i> | <i>.032</i> | <i>.033</i> | <i>.054</i> | <i>.050</i> | <i>.045</i> | <i>.033</i> | <i>.031</i> | <i>.069</i> |
| MM09_{hard} | [GABA] | - | - | - | - | - | - | 0.195 | 0.189 | 0.106 |
| | | | | | | | | <i>.034</i> | <i>.032</i> | <i>.060</i> |
| MM09_{soft} | [GABA] | - | - | - | - | - | - | 0.152 | 0.154 | 0.098 |
| | | | | | | | | <i>.03</i> | <i>.031</i> | <i>.072</i> |

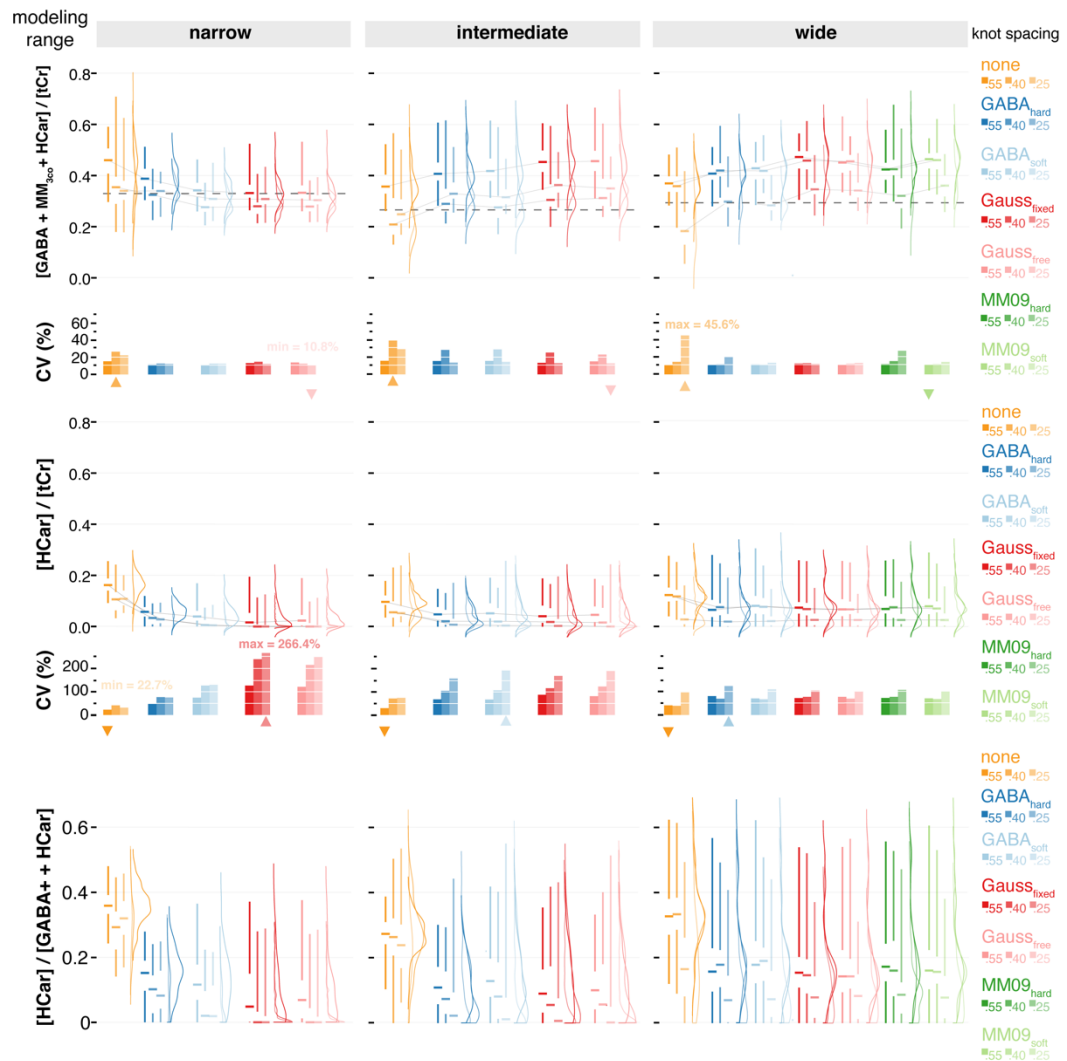
Supplementary Material 5 – MM_{3co} mean and SDs for all modeling strategies (ratios to tCr). Significant differences ($p < .05$) between the corresponding model and $GABA_{soft}$ model (gray shade) are indicated in bold.

| modeling range | | narrow | | | intermediate | | | wide | | |
|--------------------|----------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| knot spacing (ppm) | | 0.55 | 0.4 | 0.25 | 0.55 | 0.4 | 0.25 | 0.55 | 0.4 | 0.25 |
| none | [MM_{3co}] | - | - | - | - | - | - | - | - | - |
| $GABA_{hard}$ | [MM_{3co}] | - | - | - | - | - | - | - | - | - |
| $GABA_{soft}$ | [MM_{3co}] | 0.19 .026 | 0.165 .025 | 0.186 .027 | 0.210 .038 | 0.148 .033 | 0.175 .024 | 0.172 .039 | 0.194 .032 | 0.156 .032 |
| $Gauss_{fixed}$ | [MM_{3co}] | 0.233 .039 | 0.192 .038 | 0.223 .041 | 0.237 .048 | 0.192 .03 | 0.215 .035 | 0.233 .054 | 0.237 .045 | 0.235 .053 |
| $Gauss_{free}$ | [MM_{3co}] | 0.226 .038 | 0.198 .036 | 0.22 .045 | 0.229 .044 | 0.193 .031 | 0.213 .035 | 0.227 .057 | 0.237 .042 | 0.234 .053 |
| $MM09_{hard}$ | [MM_{3co}] | - | - | - | - | - | - | 0.201 .032 | 0.232 .043 | 0.240 .040 |
| $MM09_{soft}$ | [MM_{3co}] | - | - | - | - | - | - | 0.216 .051 | 0.232 .037 | 0.240 .045 |



Supplementary Material 6 – Mean modeling results and homocarnosine estimates for all modeling strategies with homocarnosine. A substantial structured residual is visible at 3 ppm if for all modeling strategies and for the narrow and intermediate modeling range the homocarnosine concentrations are significantly lower compared to omitting the co-edited MM, especially for knot spacings ≤ 0.4 ppm. All three modeling ranges (columns), three spline knot spacings (rows), and MM_{3co} model (color-coded) are

presented with mean residuals and fits, as well as the GABA, MM_{3co} , homocarnosine (HCar) and spline baseline models. The mean data is included in black. The arrows indicate the range of values for a specific modeling range and spline knot spacing with the color corresponding to the MM_{3co} model with minimum/maximum value.



Supplementary Material 7 - Distribution of GABA+ plus HCar and HCar estimates and the relative contribution of HCar to GABA+ plus HCar for all modeling strategies. The mean estimates of GABA+ plus HCar across the three spline knot spacings of the 'none' approach are indicated as a dashed line for each modeling range. All three modeling ranges (column) and three spline knot spacings (within each column), and MM_{3co} models (color-coded) are presented. Distributions are shown as half-violins (smoothed distribution), box plots with median, interquartile range, and 25th/75th quartile. The median lines of the box plots are connected to visualize trends within a specific baseline knot spacing. CVs are

summarized as bar plots. Minimum/maximum CVs for each spline knot spacing are indicated as downwards/upwards triangles in the color corresponding to the MM_{3co} model. Global minimum and maximum CVs across all models are added as text.