Getting Started with tcaCALC

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tcaCALC

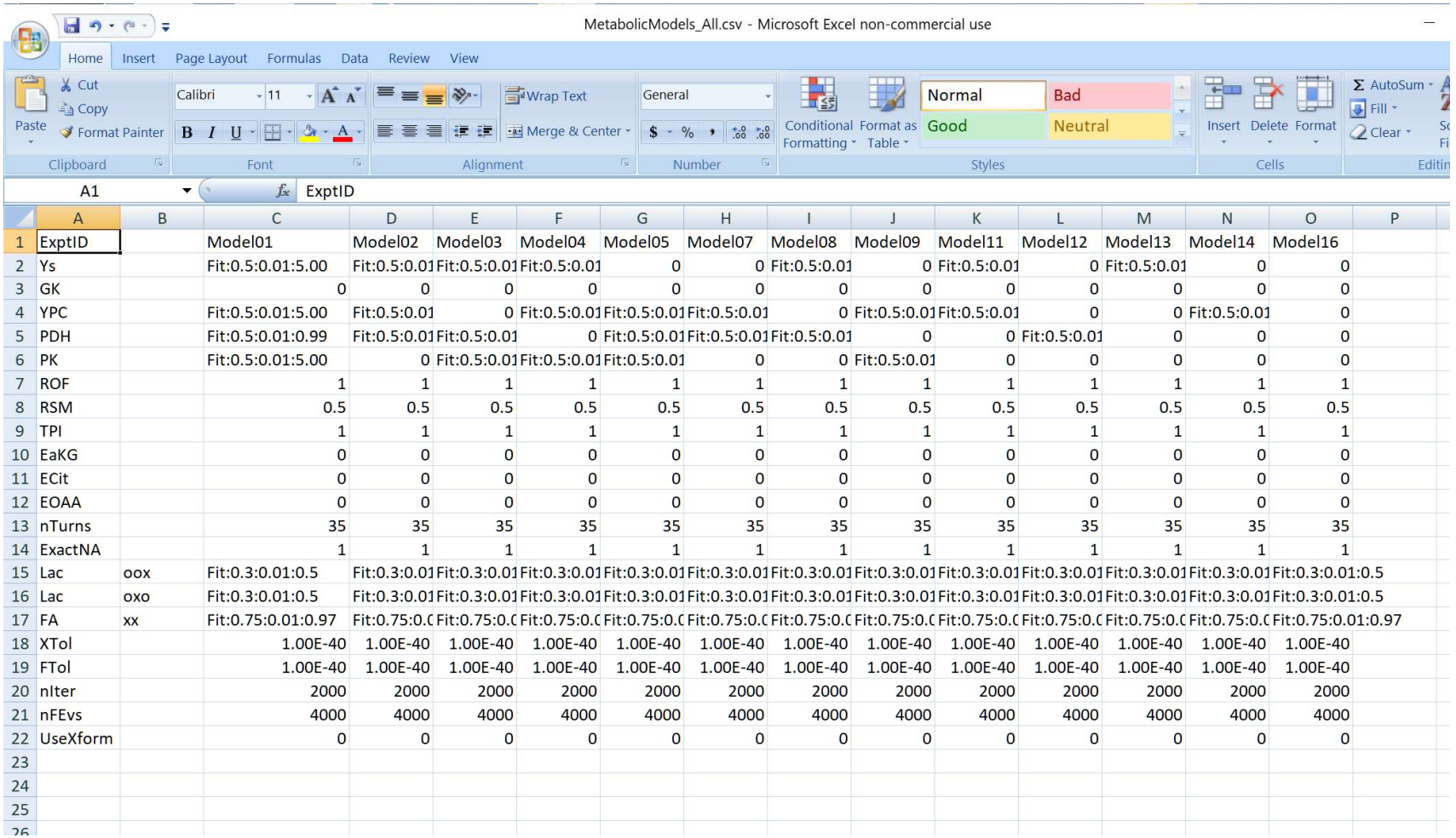
- The tcaCALC software tool is designed to determine best fit metabolic fluxes in studies that use ^{13}C- or ^{14}C-enriched tracers to probe TCA cycle metabolism.
- The newest version of tcaCALC was written in MATLAB.
  - MATLAB assures compatibility across multiple operating system platforms.
  - tcaCALC is based on previous versions that were written in the C programming language and ran only under the now obsolete Microsoft Disk Operating System.
- The user submits measured values of specific atom fractional enrichments, ^{13}C NMR multiplet relative integrated intensities, or relative mass isotopologue intensities of common products of TCA cycle metabolism together with the substrate isotopic enrichment that was used in a particular experiment.
- tcaCALC iteratively determines the PDH, YPC, YS and PK rates (relative to citrate synthase) that best fit the measured data.

User-input: Two methods

- tcaCALC can be run with user-input
  - from GUI (General User Interface) or
  - from two user-generated comma-separated-value (CSV) spreadsheets.
- The GUI method is useful for learning and understanding software but is cumbersome when complex studies need to be analyzed
- This presentation is focussed on user-input via the csv spreadsheet

Create a CSV spreadsheet that describes the hypothetical metabolic models

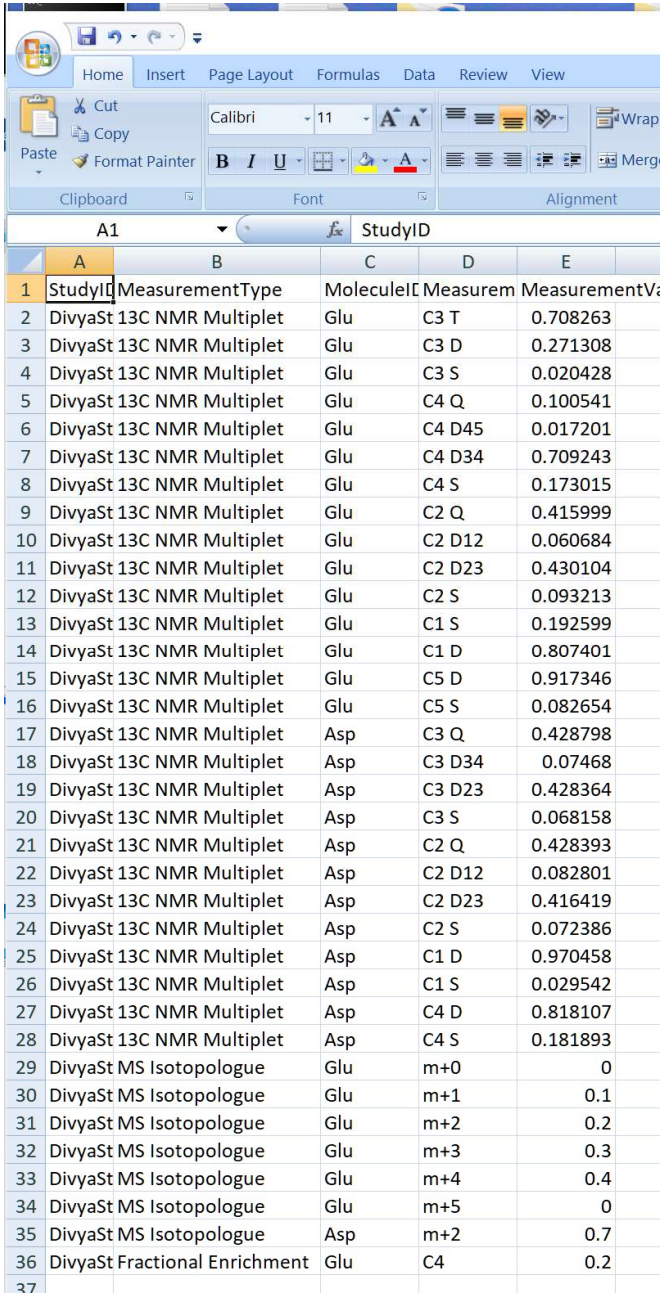
- An example csv is provided at .\InputTemplates\MetabolicModelInput\MetabolicModels_All.csv



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1	ExptID		Model01	Model02	Model03	Model04	Model05	Model07	Model08	Model09	Model11	Model12	Model13	Model14	Model16	
2	Ys		Fit:0.5:0.01:5.00	Fit:0.5:0.01	Fit:0.5:0.01	Fit:0.5:0.01	0	0	Fit:0.5:0.01	0	Fit:0.5:0.01	0	Fit:0.5:0.01	0	0	
3	GK		0	0	0	0	0	0	0	0	0	0	0	0	0	
4	YPC		Fit:0.5:0.01:5.00	Fit:0.5:0.01	0	Fit:0.5:0.01	Fit:0.5:0.01	Fit:0.5:0.01	0	Fit:0.5:0.01	Fit:0.5:0.01	0	0	Fit:0.5:0.01	0	
5	PDH		Fit:0.5:0.01:0.99	Fit:0.5:0.01	Fit:0.5:0.01	0	Fit:0.5:0.01	Fit:0.5:0.01	Fit:0.5:0.01	0	0	Fit:0.5:0.01	0	0	0	
6	PK		Fit:0.5:0.01:5.00	0	Fit:0.5:0.01	Fit:0.5:0.01	Fit:0.5:0.01	0	0	Fit:0.5:0.01	0	0	0	0	0	
7	ROF		1	1	1	1	1	1	1	1	1	1	1	1	1	
8	RSM		0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	
9	TPI		1	1	1	1	1	1	1	1	1	1	1	1	1	
10	EaKG		0	0	0	0	0	0	0	0	0	0	0	0	0	
11	ECit		0	0	0	0	0	0	0	0	0	0	0	0	0	
12	EOAA		0	0	0	0	0	0	0	0	0	0	0	0	0	
13	nTurns		35	35	35	35	35	35	35	35	35	35	35	35	35	
14	ExactNA		1	1	1	1	1	1	1	1	1	1	1	1	1	
15	Lac	oox	Fit:0.3:0.01:0.5	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01:0.5	
16	Lac	oxo	Fit:0.3:0.01:0.5	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01	Fit:0.3:0.01:0.5	
17	FA	xx	Fit:0.75:0.01:0.97	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.(	Fit:0.75:0.01:0.97	
18	XTol		1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	
19	FTol		1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	1.00E-40	
20	nIter		2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	
21	nFEvs		4000	4000	4000	4000	4000	4000	4000	4000	4000	4000	4000	4000	4000	
22	UseXform		0	0	0	0	0	0	0	0	0	0	0	0	0	
23																
24																
25																
26																

Create a CSV spreadsheet that describes the measured data

- An example csv is provided at .\InputTemplates\GDAInput\GeneralDataArrayInput.csv
- Legal entries for MoleculeID and Measures columns in this spreadsheet are given in .\InputTemplates\GDAInput\ LegalGDAEntries.txt



Home Insert Page Layout Formulas Data Review View

Cut Copy Format Painter Paste Clipboard

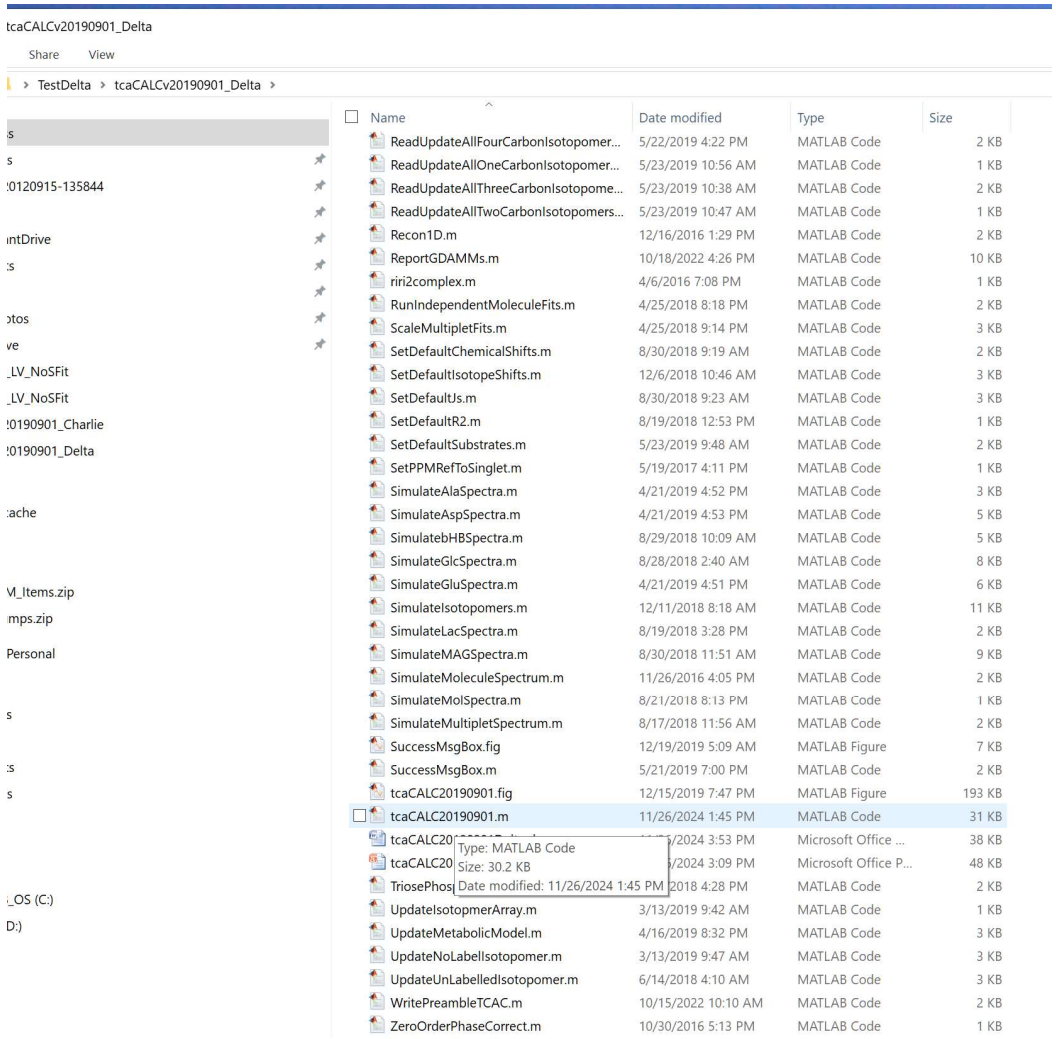
Calibri 11 Font Alignment Wrap

A1 StudyID

	A	B	C	D	E
1	StudyID	MeasurementType	MoleculeID	Measurem	MeasurementVa
2	DivyaSt	13C NMR Multiplet	Glu	C3 T	0.708263
3	DivyaSt	13C NMR Multiplet	Glu	C3 D	0.271308
4	DivyaSt	13C NMR Multiplet	Glu	C3 S	0.020428
5	DivyaSt	13C NMR Multiplet	Glu	C4 Q	0.100541
6	DivyaSt	13C NMR Multiplet	Glu	C4 D45	0.017201
7	DivyaSt	13C NMR Multiplet	Glu	C4 D34	0.709243
8	DivyaSt	13C NMR Multiplet	Glu	C4 S	0.173015
9	DivyaSt	13C NMR Multiplet	Glu	C2 Q	0.415999
10	DivyaSt	13C NMR Multiplet	Glu	C2 D12	0.060684
11	DivyaSt	13C NMR Multiplet	Glu	C2 D23	0.430104
12	DivyaSt	13C NMR Multiplet	Glu	C2 S	0.093213
13	DivyaSt	13C NMR Multiplet	Glu	C1 S	0.192599
14	DivyaSt	13C NMR Multiplet	Glu	C1 D	0.807401
15	DivyaSt	13C NMR Multiplet	Glu	C5 D	0.917346
16	DivyaSt	13C NMR Multiplet	Glu	C5 S	0.082654
17	DivyaSt	13C NMR Multiplet	Asp	C3 Q	0.428798
18	DivyaSt	13C NMR Multiplet	Asp	C3 D34	0.07468
19	DivyaSt	13C NMR Multiplet	Asp	C3 D23	0.428364
20	DivyaSt	13C NMR Multiplet	Asp	C3 S	0.068158
21	DivyaSt	13C NMR Multiplet	Asp	C2 Q	0.428393
22	DivyaSt	13C NMR Multiplet	Asp	C2 D12	0.082801
23	DivyaSt	13C NMR Multiplet	Asp	C2 D23	0.416419
24	DivyaSt	13C NMR Multiplet	Asp	C2 S	0.072386
25	DivyaSt	13C NMR Multiplet	Asp	C1 D	0.970458
26	DivyaSt	13C NMR Multiplet	Asp	C1 S	0.029542
27	DivyaSt	13C NMR Multiplet	Asp	C4 D	0.818107
28	DivyaSt	13C NMR Multiplet	Asp	C4 S	0.181893
29	DivyaSt	MS Isotopologue	Glu	m+0	0
30	DivyaSt	MS Isotopologue	Glu	m+1	0.1
31	DivyaSt	MS Isotopologue	Glu	m+2	0.2
32	DivyaSt	MS Isotopologue	Glu	m+3	0.3
33	DivyaSt	MS Isotopologue	Glu	m+4	0.4
34	DivyaSt	MS Isotopologue	Glu	m+5	0
35	DivyaSt	MS Isotopologue	Asp	m+2	0.7
36	DivyaSt	Fractional Enrichment	Glu	C4	0.2
37					

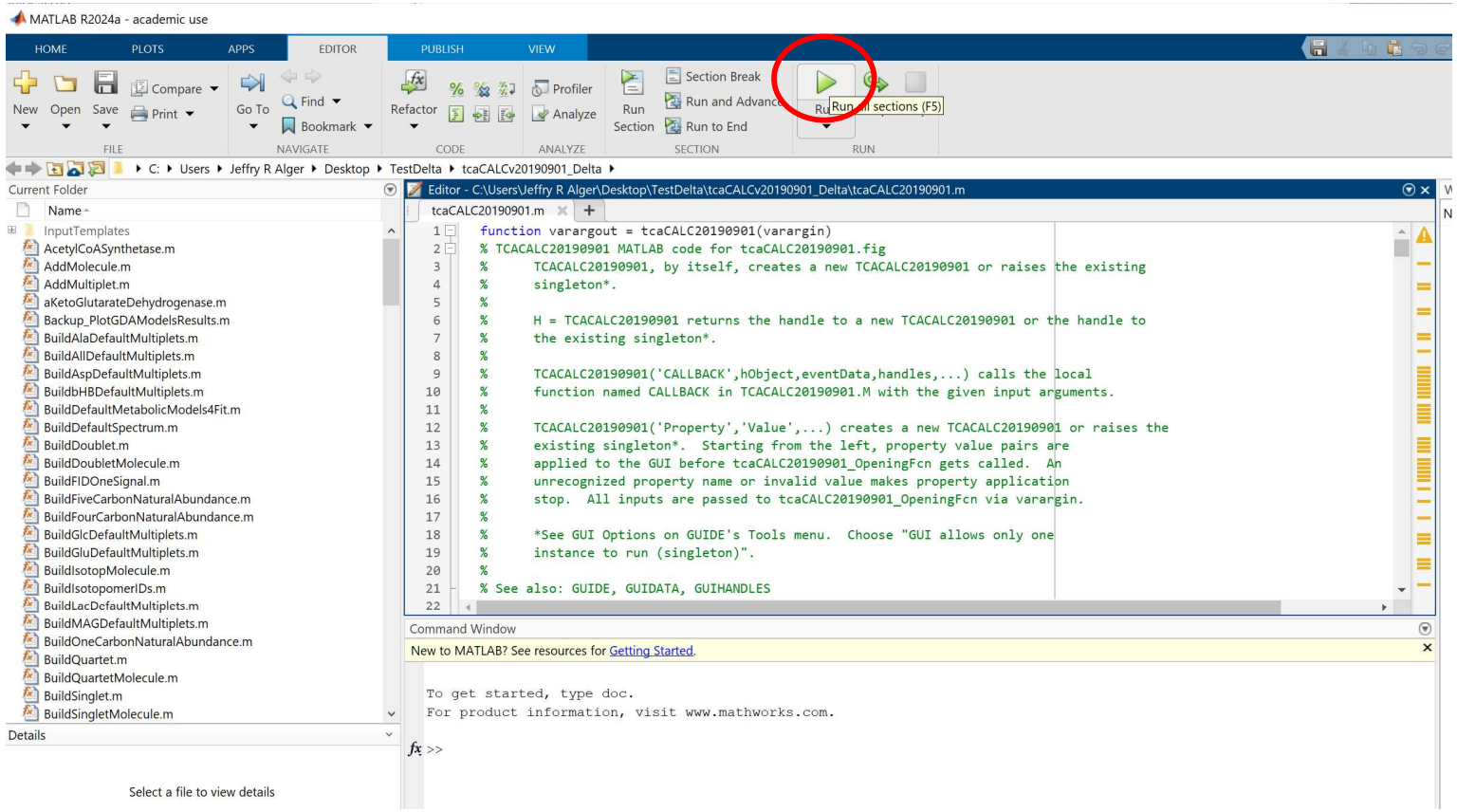
Start tcaCALC software

- Open the tcaCALC distribution folder
- Select tcaCALC20190901.m
- MATLAB will open



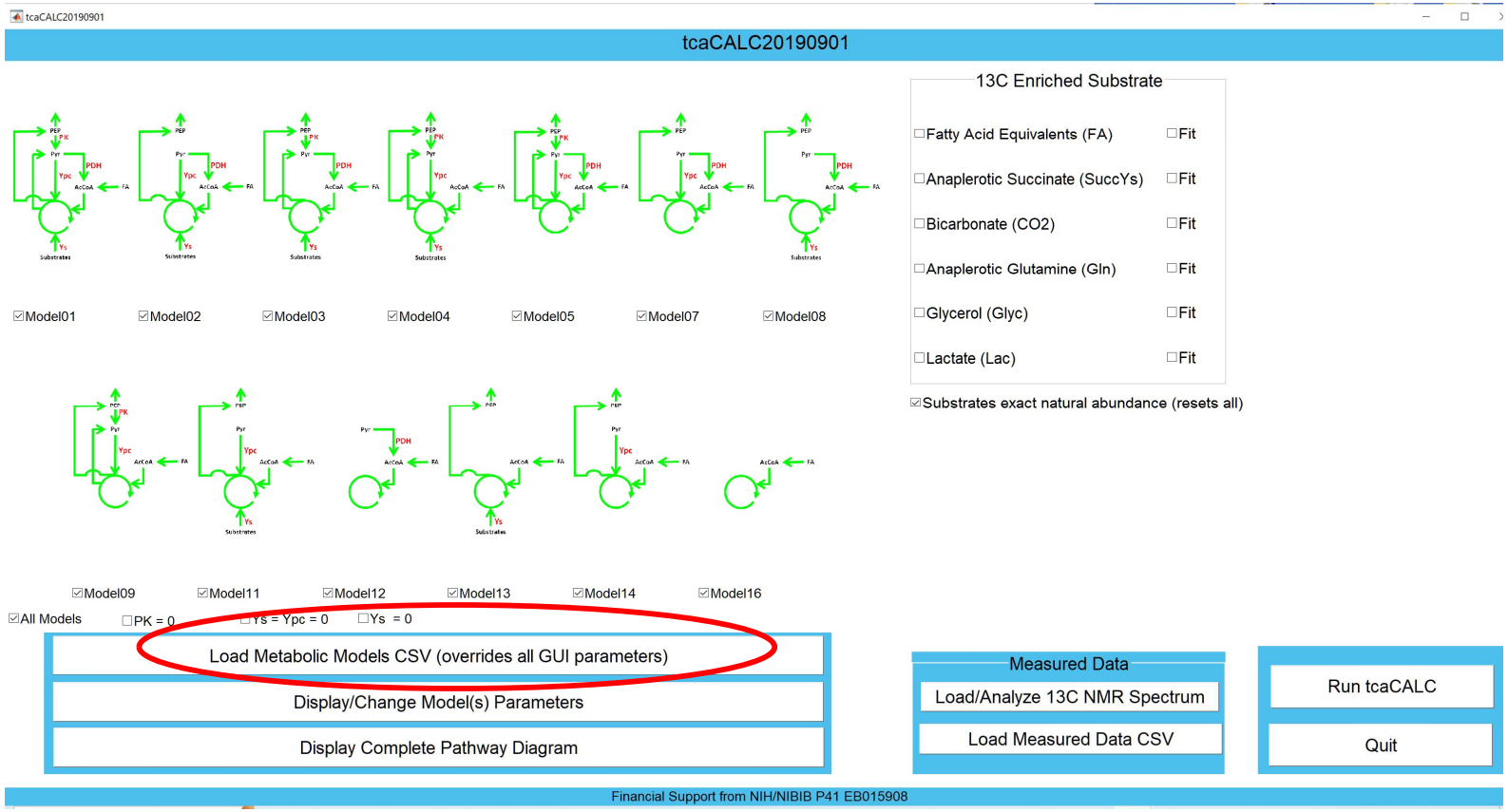
Run tcaCALC with MATLAB

- Select the green arrow in the MATLAB editor to run the tcaCLAC software
- The tcaCALC GUI will open



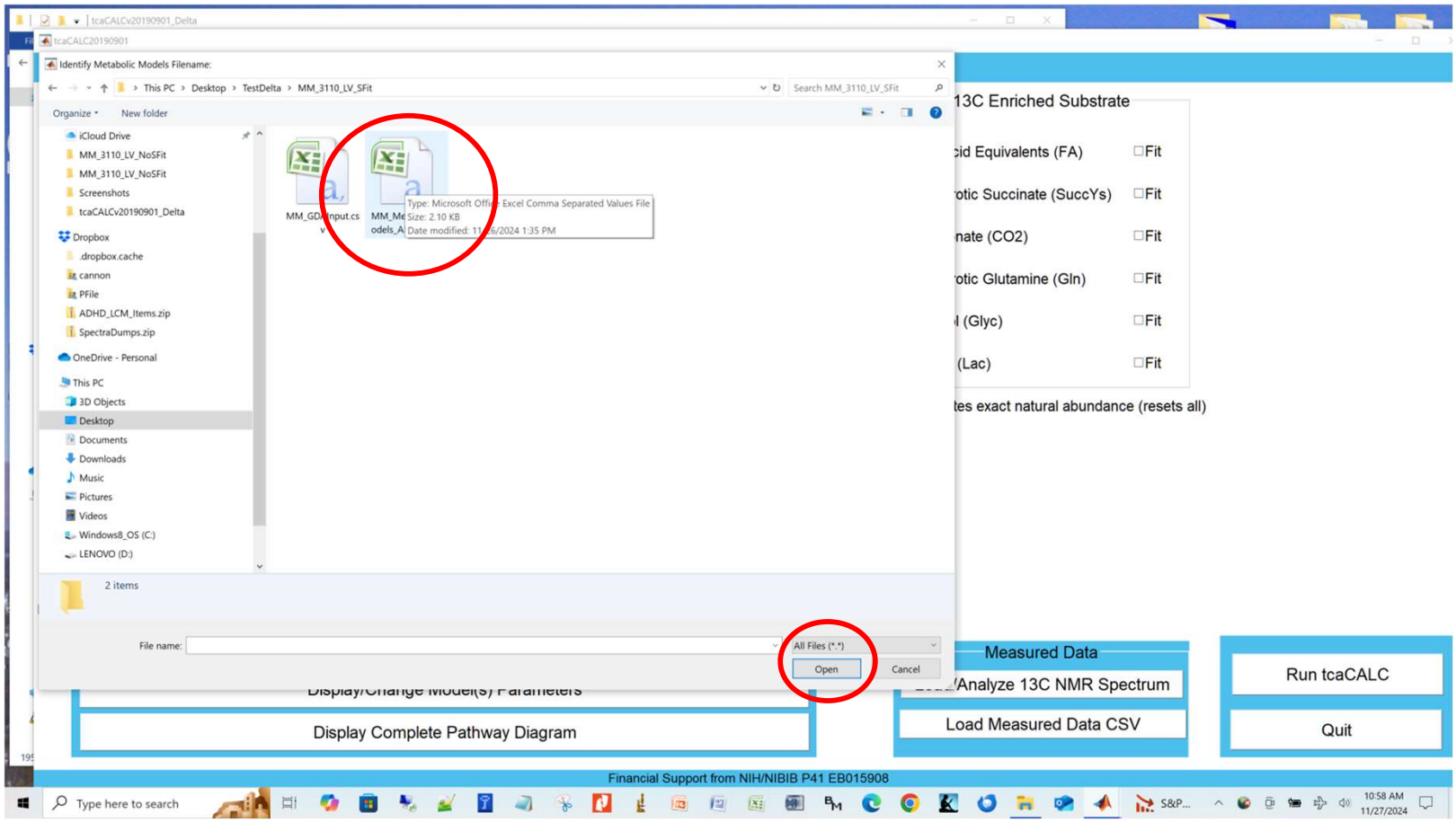
Input the Metabolic Models

- Select Load Metabolic Models …



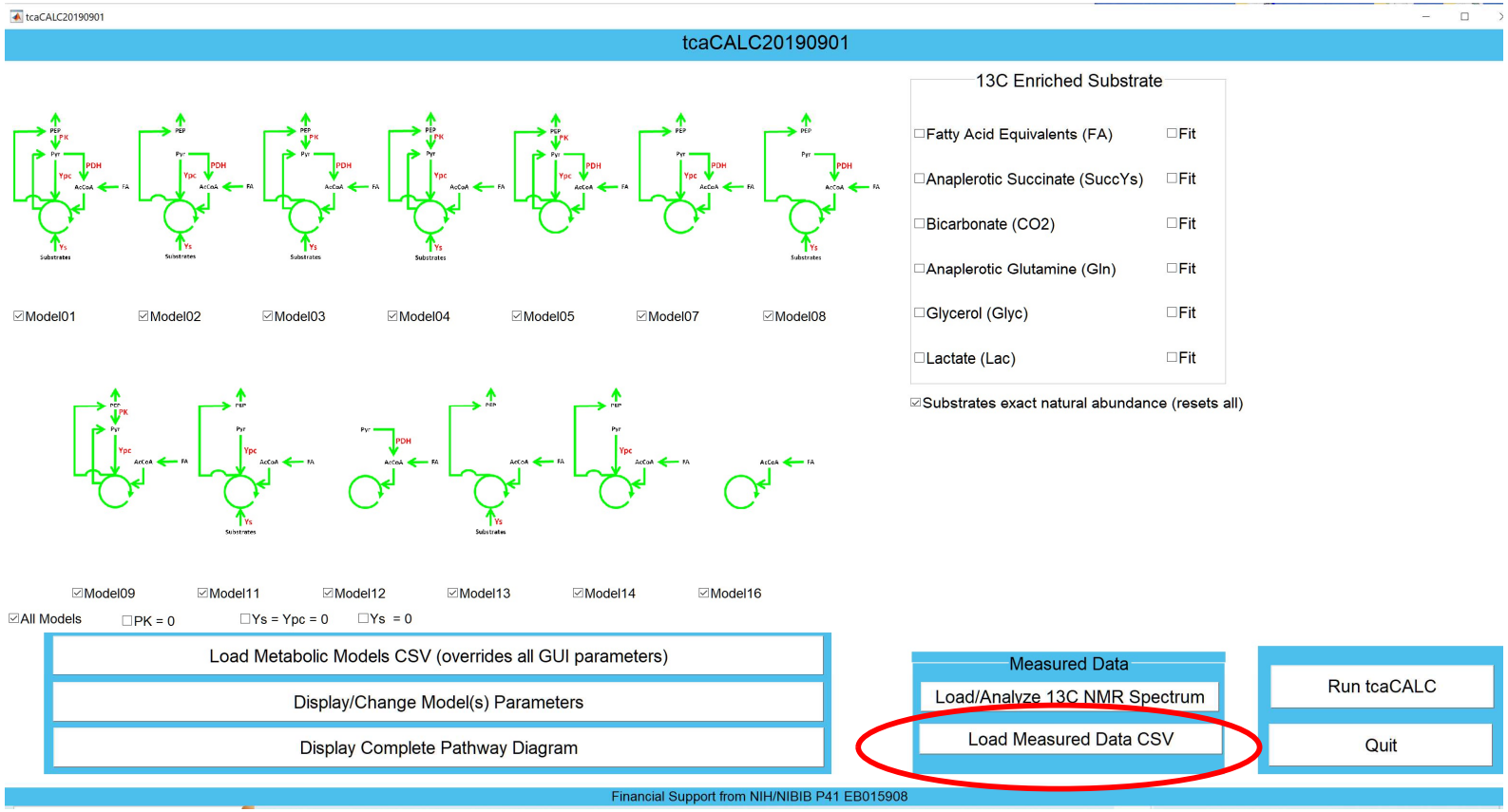
Input the Metabolic Models

- Navigate to and select the metabolic models csv



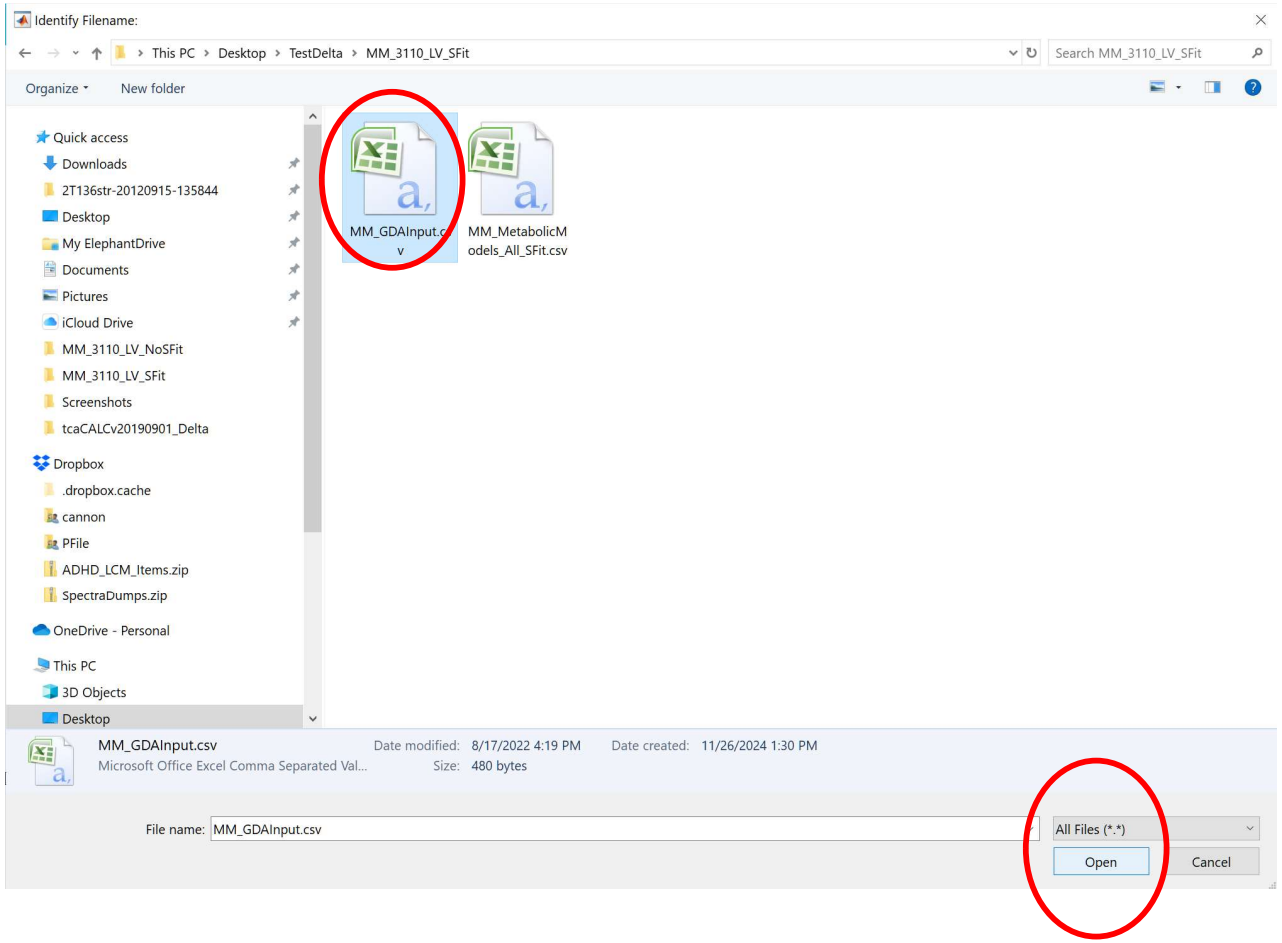
Input the measured data

- Select Load Measured Data CSV



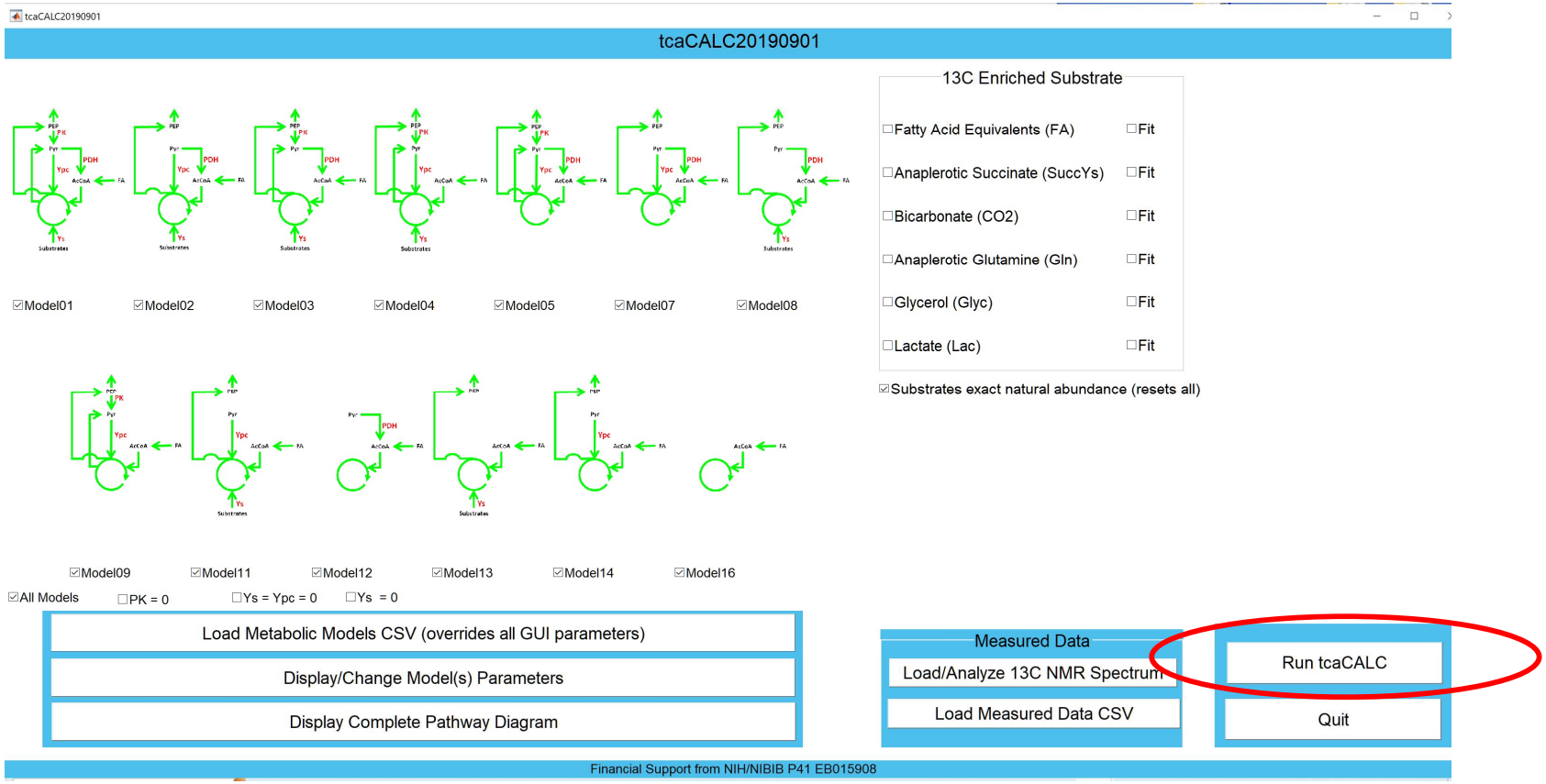
Input the measured data

- Navigate to and select the measured data csv



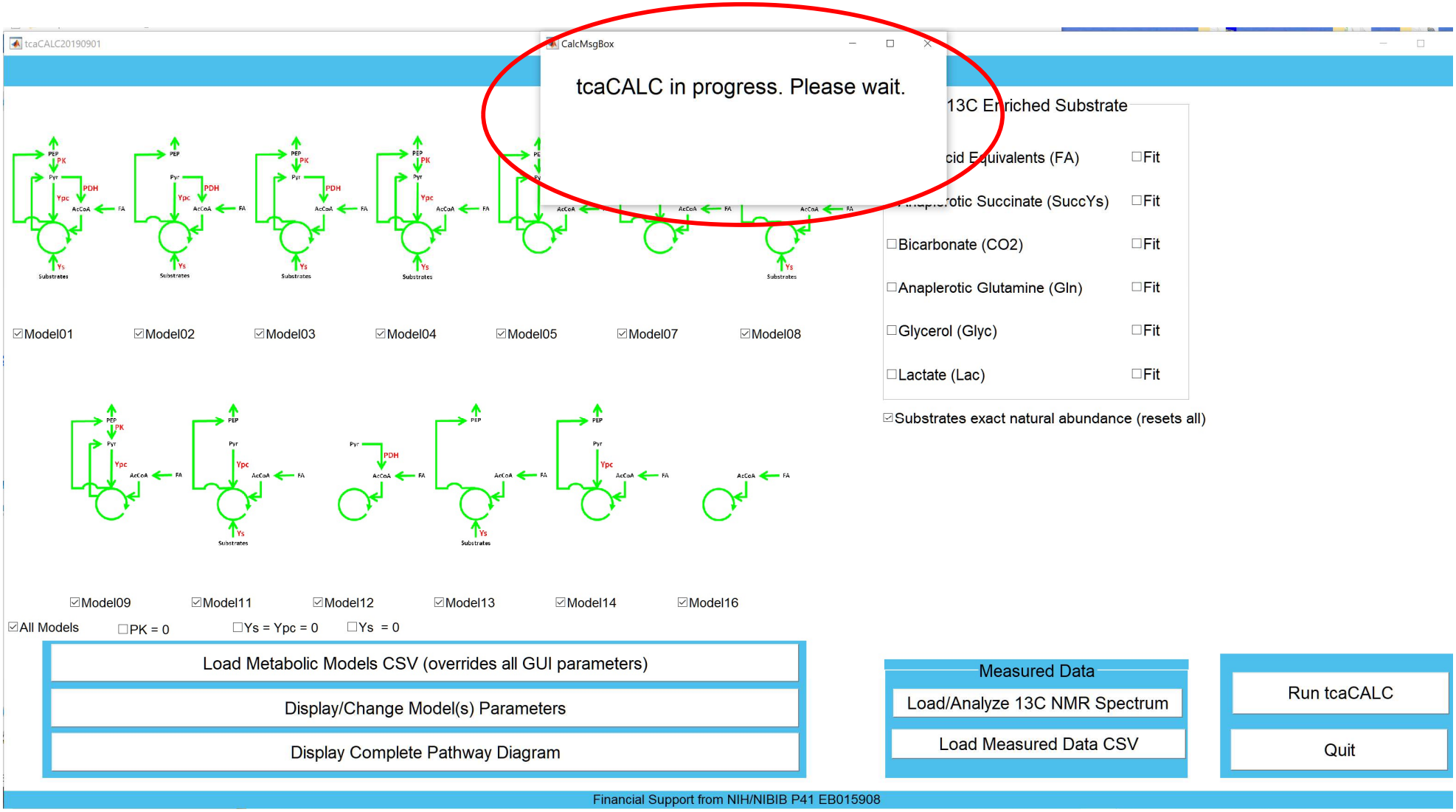
Run tcaCALC

- Select Run tcaCALC



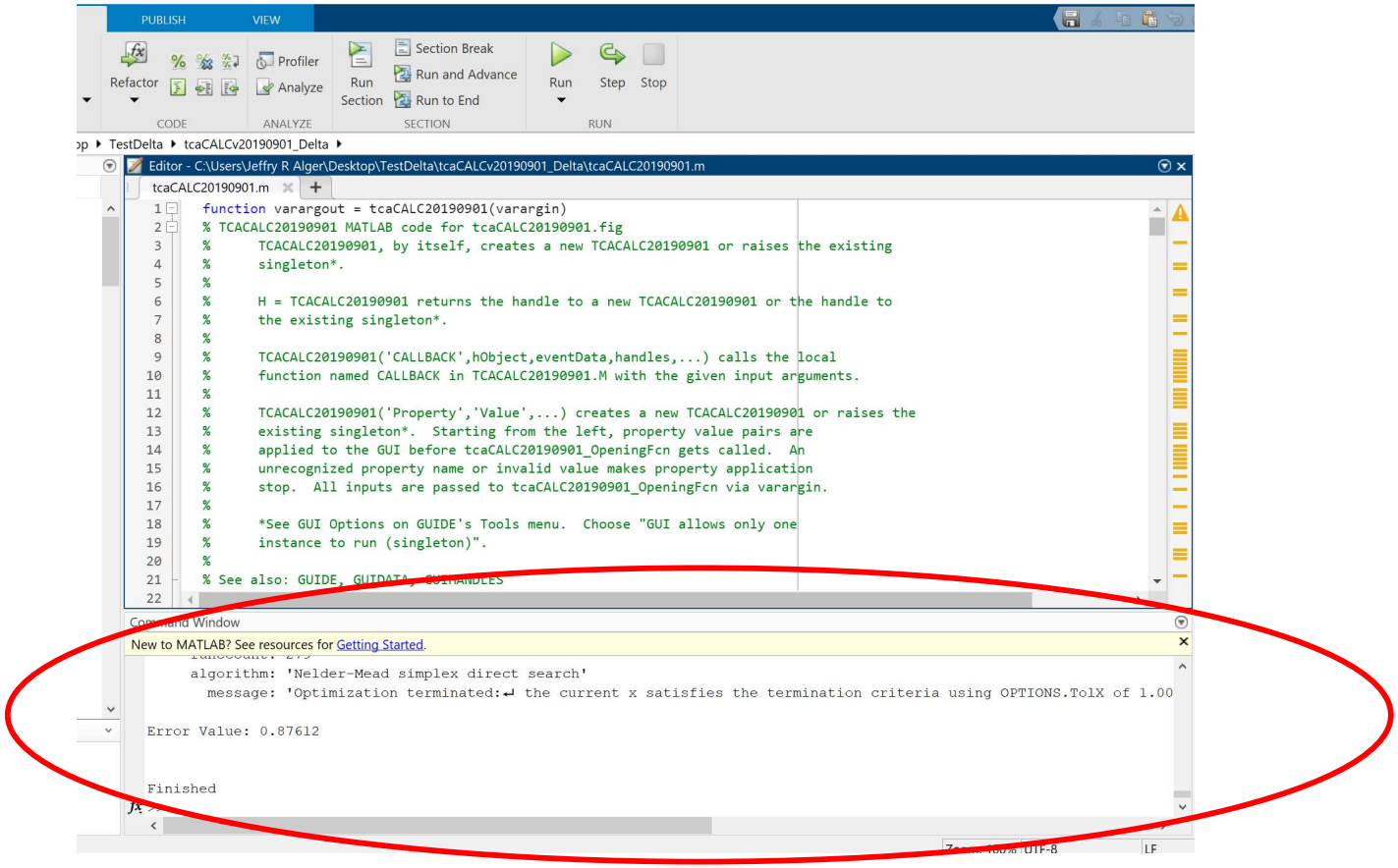
Run tcaCALC

- tcaCALC in progress window appears



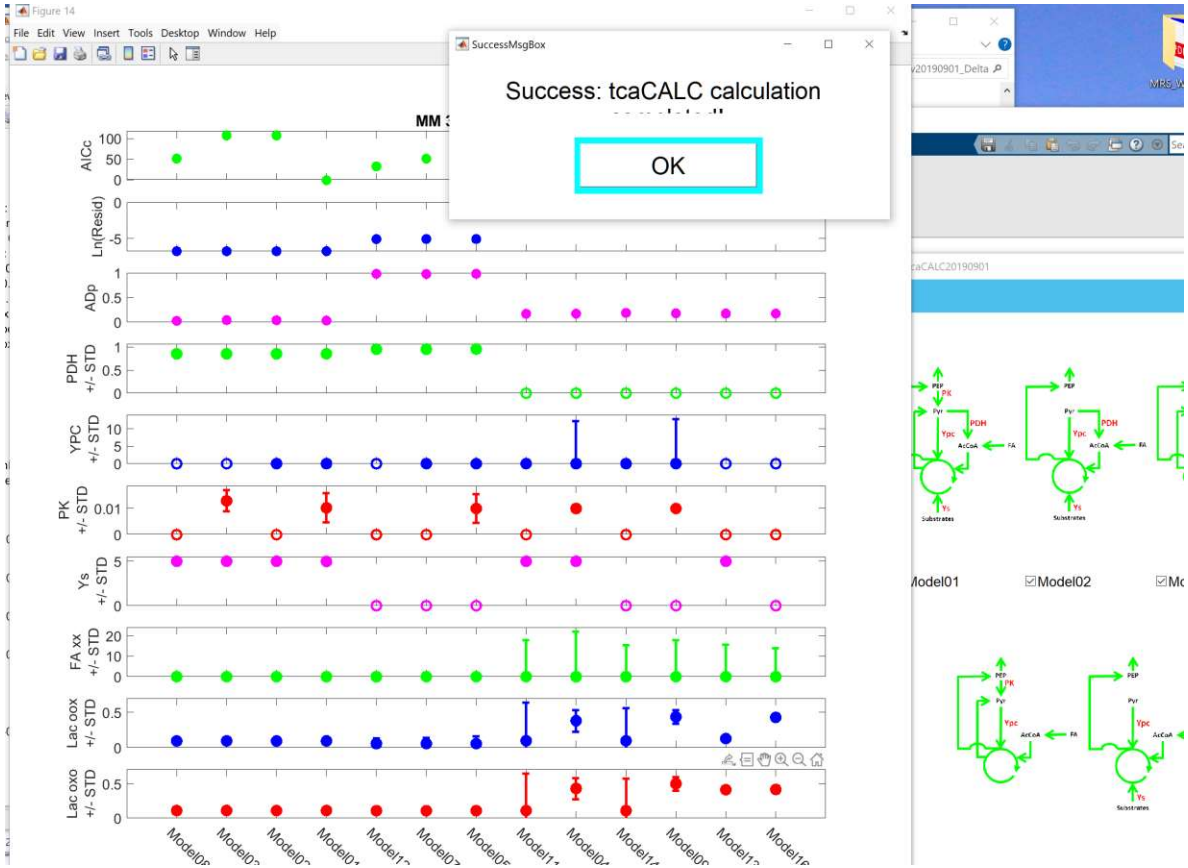
Run tcaCALC

- Monitor tcaCALC in MATLAB window (if desired)



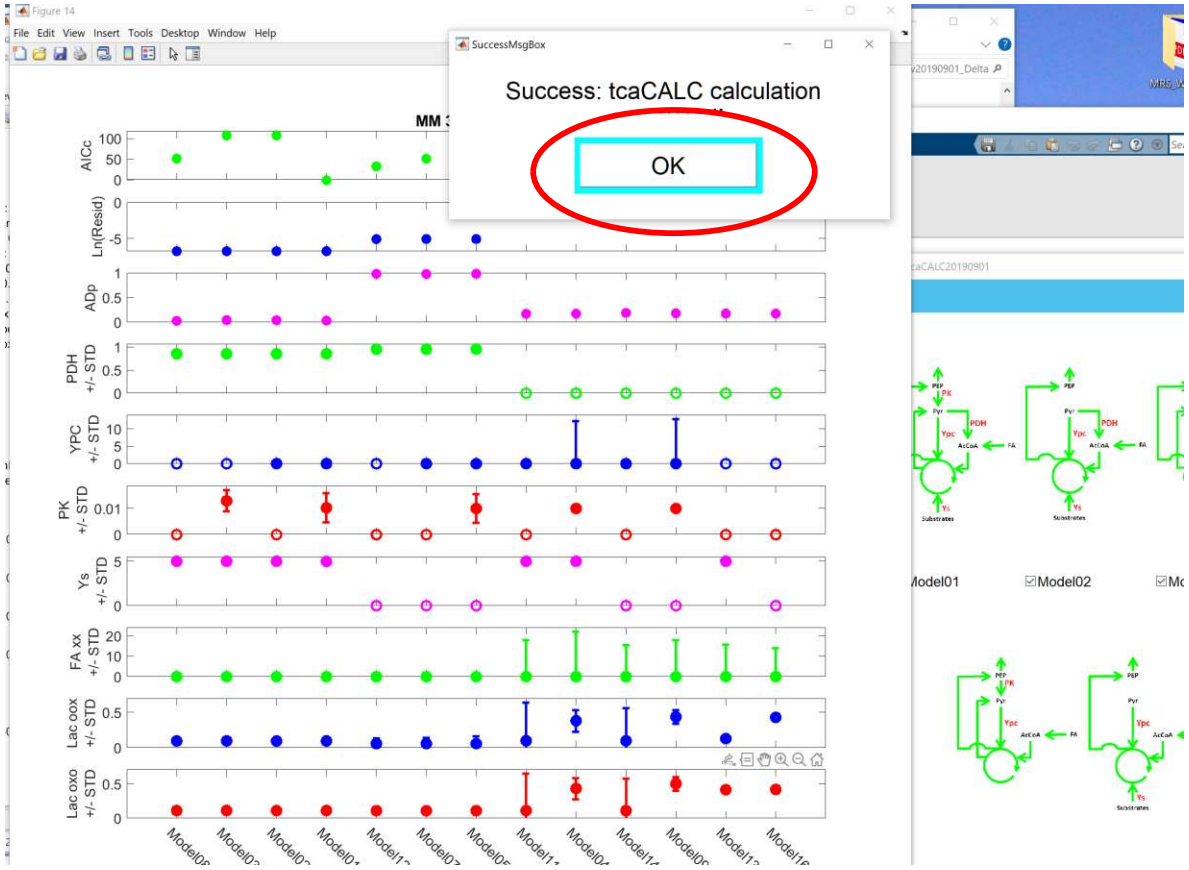
tcaCALC completion

- On completion tcaCALC presents results as graphics



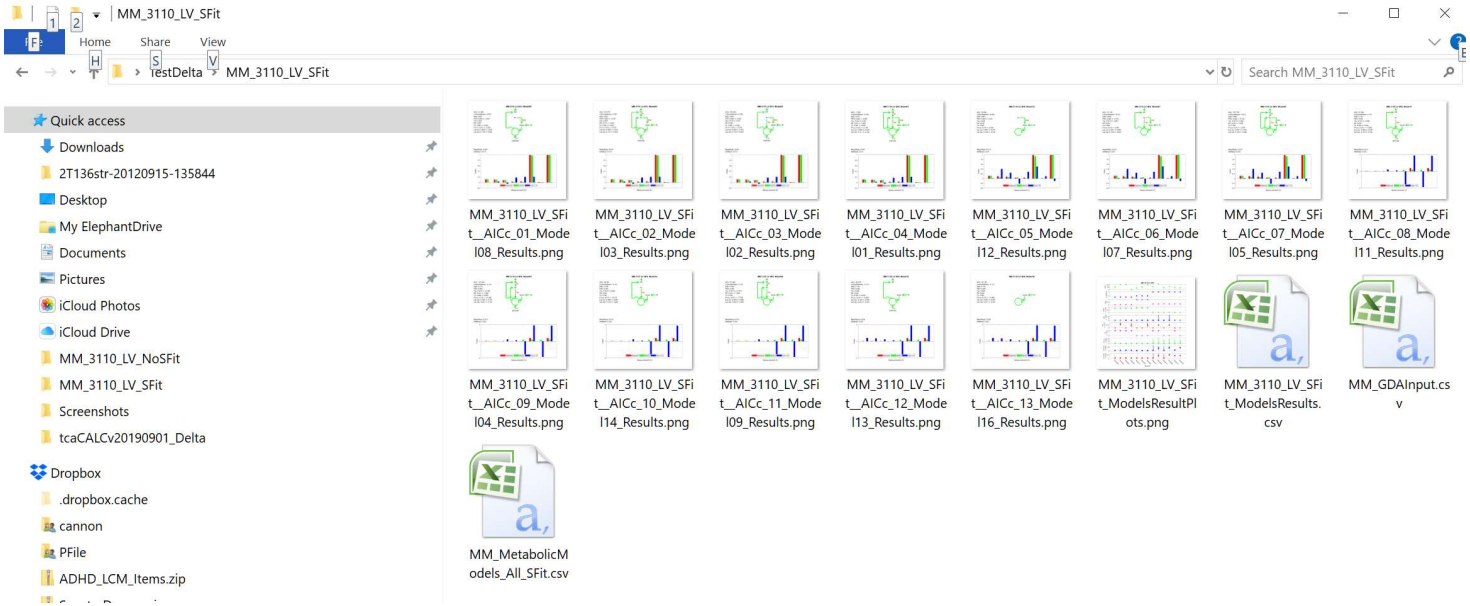
tcaCALC completion

- Select OK to save and close all graphics output

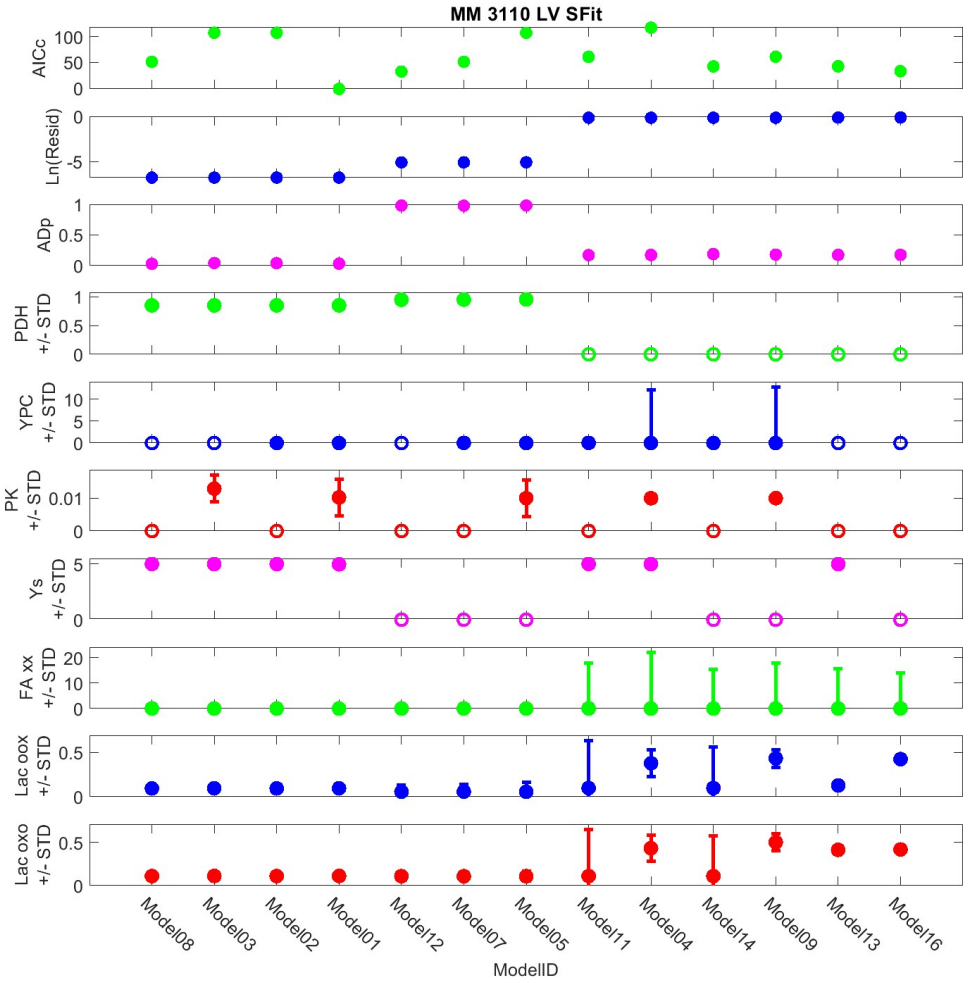


tcaCALC completion

- tcaCALC graphics and numerical results are saved to the directory that contains the Metabolic Models .csv

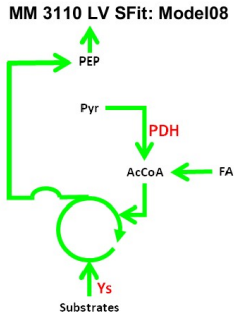


tcaCALC All Models Output Results (Graphics) Summary Plot

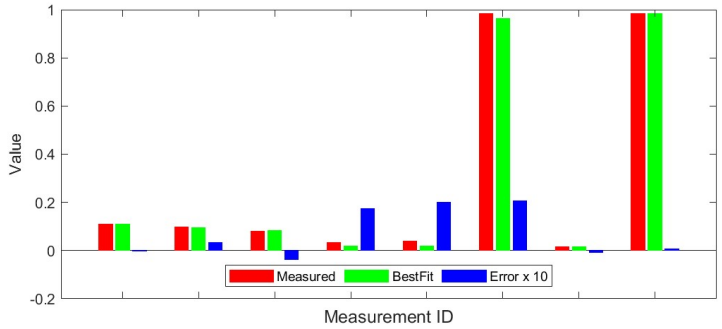


tcaCALC Model Output Results (Graphics)
One produced for Each Model

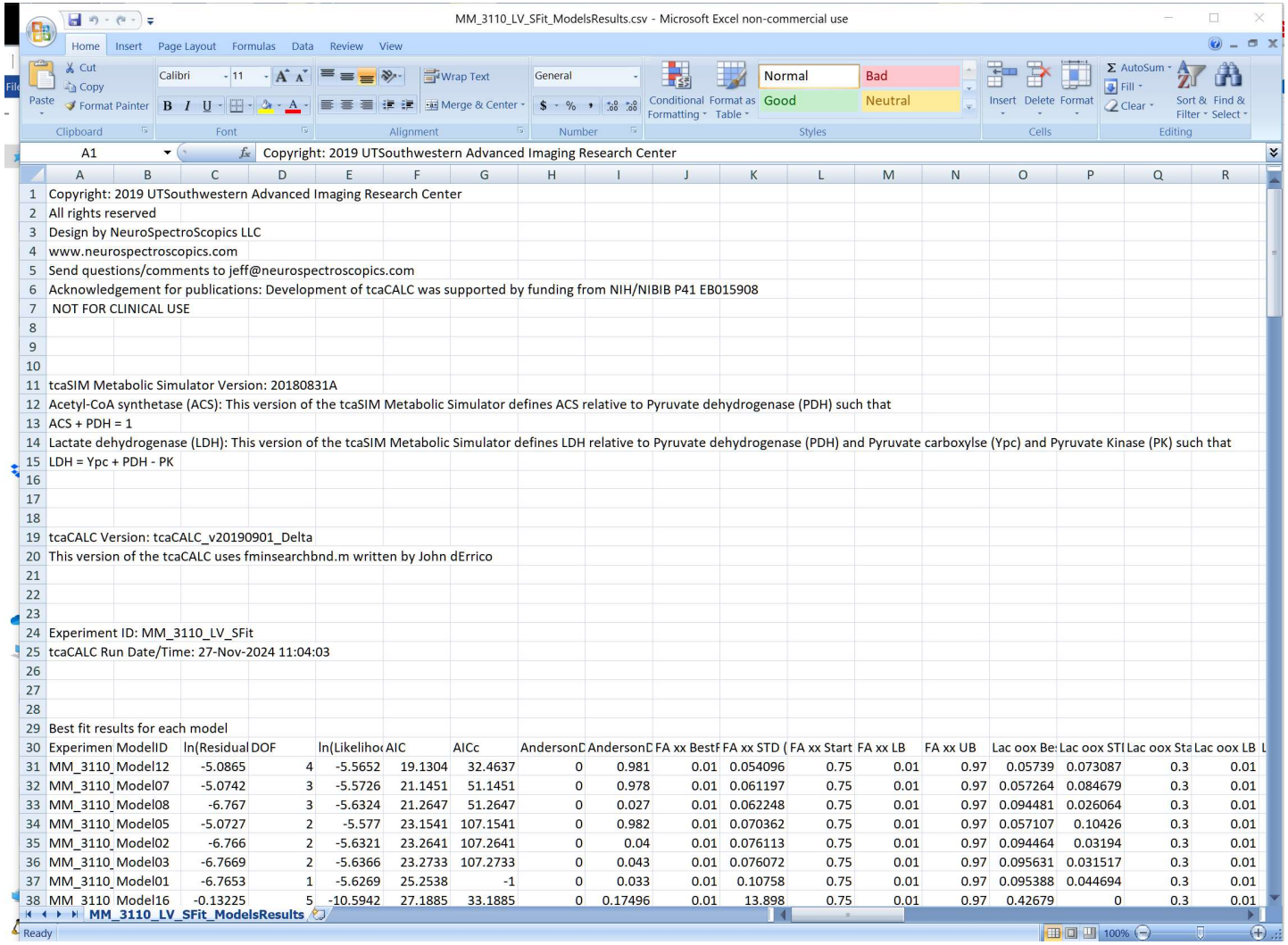
AICc: 51.265
LnSumSqResid: -6.767
ADp: 0.027
PDH: 0.852 +/- 0.005
Ypc: 0.000
PK: 0.000
Ys: 5.000 +/- 0.000
FA xx: 0.010 +/- 0.062
Lac oox: 0.094 +/- 0.026
Lac oxo: 0.110 +/- 0.020



MeanResid: 0.007
StdResid: 0.010



tcaCALC Models Output Results (Numerical)



MM_3110_LV_SFit_ModelsResults.csv - Microsoft Excel non-commercial use

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Send questions/comments to jeff@neurospectroscopics.com
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tcaSIM Metabolic Simulator Version: 20180831A
Acetyl-CoA synthetase (ACS): This version of the tcaSIM Metabolic Simulator defines ACS relative to Pyruvate dehydrogenase (PDH) such that
ACS + PDH = 1
Lactate dehydrogenase (LDH): This version of the tcaSIM Metabolic Simulator defines LDH relative to Pyruvate dehydrogenase (PDH) and Pyruvate carboxylse (Ypc) and Pyruvate Kinase (PK) such that
LDH = Ypc + PDH - PK

tcaCALC Version: tcaCALC_v20190901_Delta
This version of the tcaCALC uses fminsearchbnd.m written by John dErrico

Experiment ID: MM_3110_LV_SFit
tcaCALC Run Date/Time: 27-Nov-2024 11:04:03

Best fit results for each model

Experimen	ModelID	ln(Residual	DOF	ln(Likelihoo	AIC	AICc	AndersonD	AndersonD	FA xx BestF	FA xx STD (	FA xx Start	FA xx LB	FA xx UB	Lac oox Be	Lac oox STI	Lac oox Sta	Lac oox LB
MM_3110_	Model12	-5.0865	4	-5.5652	19.1304	32.4637	0	0.981	0.01	0.054096	0.75	0.01	0.97	0.05739	0.073087	0.3	0.01
MM_3110_	Model07	-5.0742	3	-5.5726	21.1451	51.1451	0	0.978	0.01	0.061197	0.75	0.01	0.97	0.057264	0.084679	0.3	0.01
MM_3110_	Model08	-6.767	3	-5.6324	21.2647	51.2647	0	0.027	0.01	0.062248	0.75	0.01	0.97	0.094481	0.026064	0.3	0.01
MM_3110_	Model05	-5.0727	2	-5.577	23.1541	107.1541	0	0.982	0.01	0.070362	0.75	0.01	0.97	0.057107	0.10426	0.3	0.01
MM_3110_	Model02	-6.766	2	-5.6321	23.2641	107.2641	0	0.04	0.01	0.076113	0.75	0.01	0.97	0.094464	0.03194	0.3	0.01
MM_3110_	Model03	-6.7669	2	-5.6366	23.2733	107.2733	0	0.043	0.01	0.076072	0.75	0.01	0.97	0.095631	0.031517	0.3	0.01
MM_3110_	Model01	-6.7653	1	-5.6269	25.2538	-1	0	0.033	0.01	0.10758	0.75	0.01	0.97	0.095388	0.044694	0.3	0.01
MM_3110_	Model16	-0.13225	5	-10.5942	27.1885	33.1885	0	0.17496	0.01	13.898	0.75	0.01	0.97	0.42679	0	0.3	0.01

MM_3110_LV_SFit_ModelsResults
Ready