

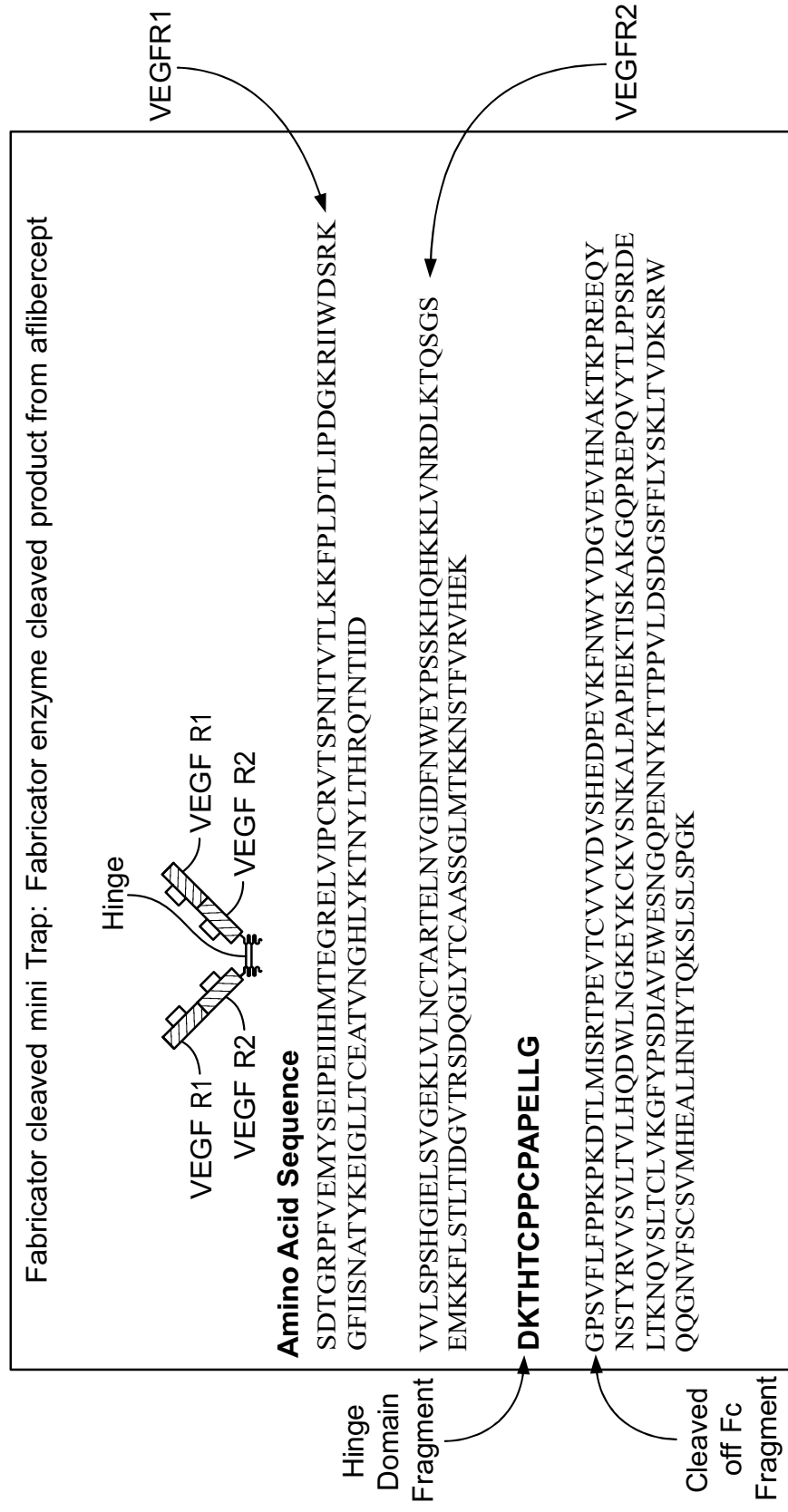


FIG.1

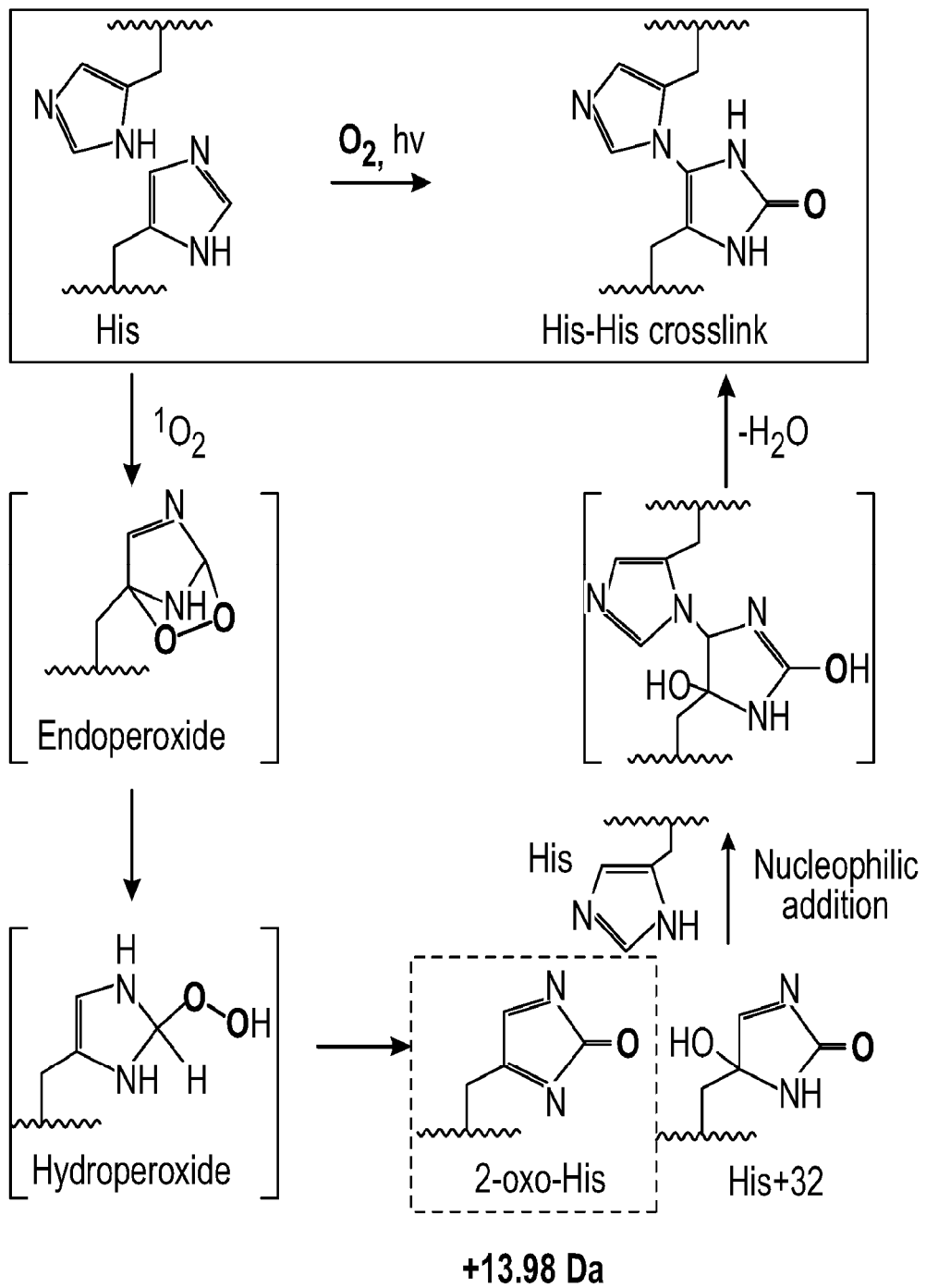
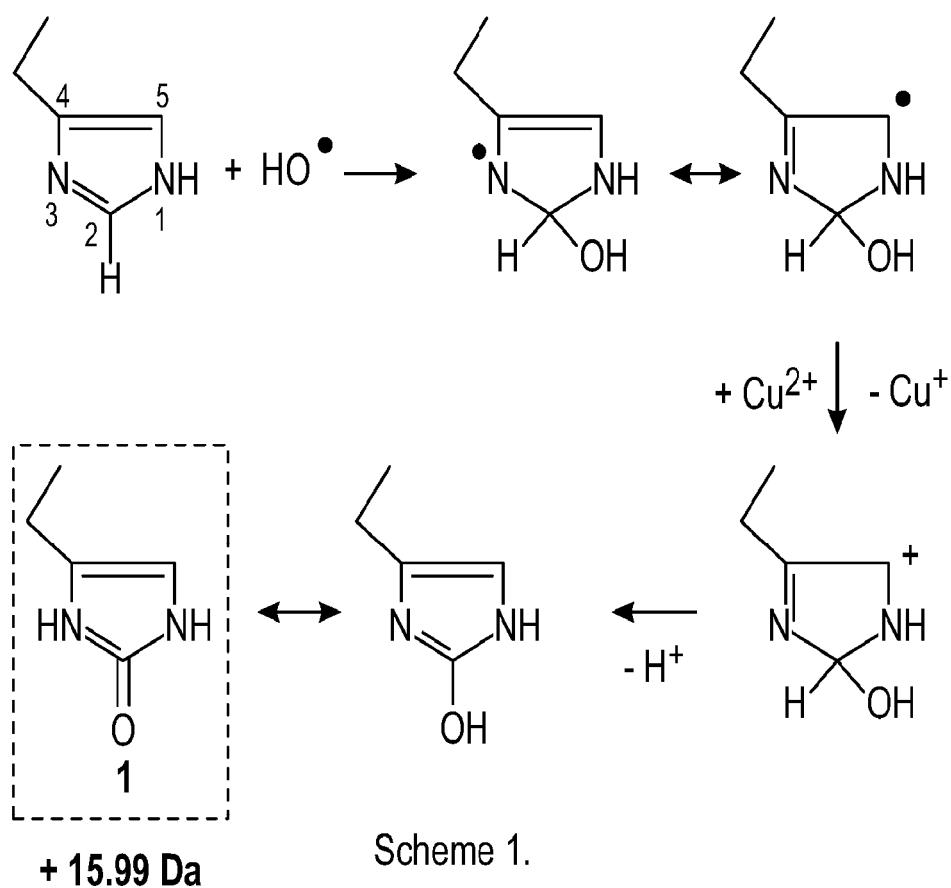


FIG. 2

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Scheme 1.

FIG. 3

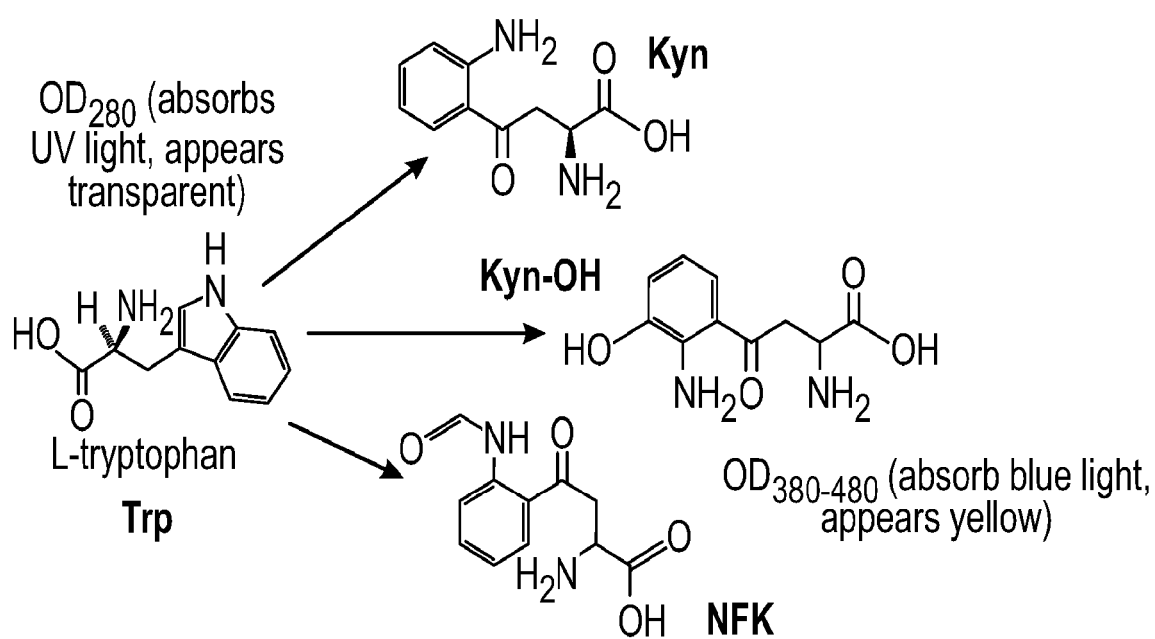
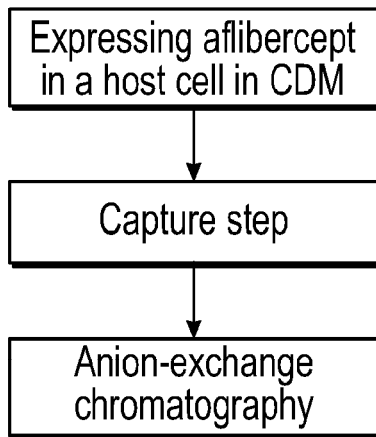
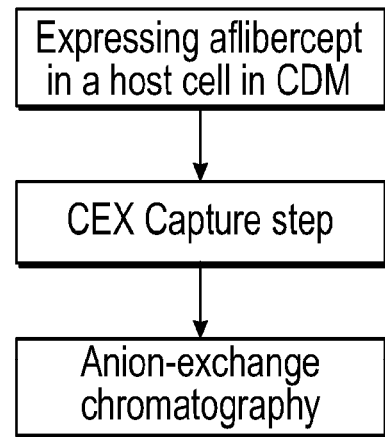
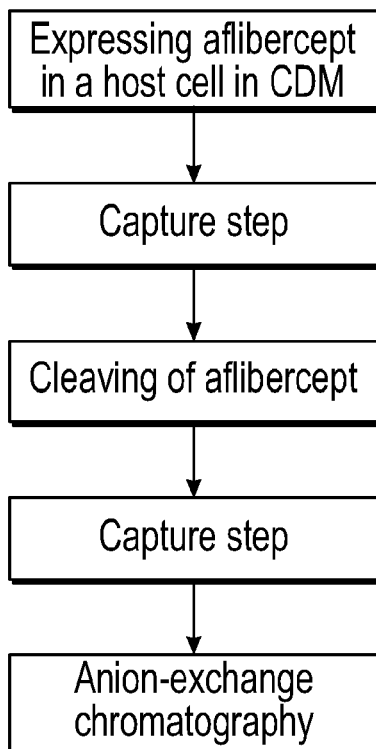
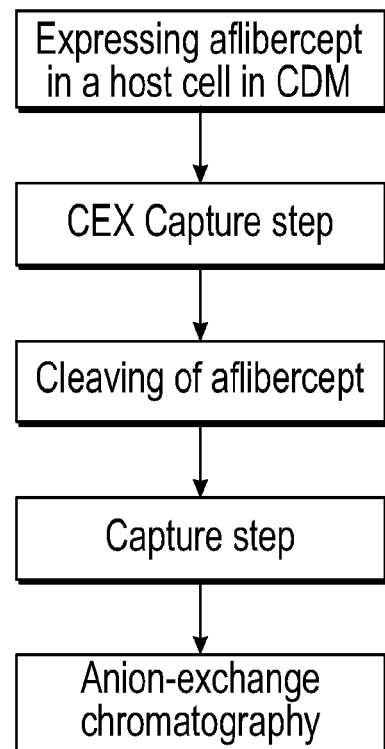


FIG. 4

**FIG. 5****FIG. 7****FIG. 6****FIG. 8**

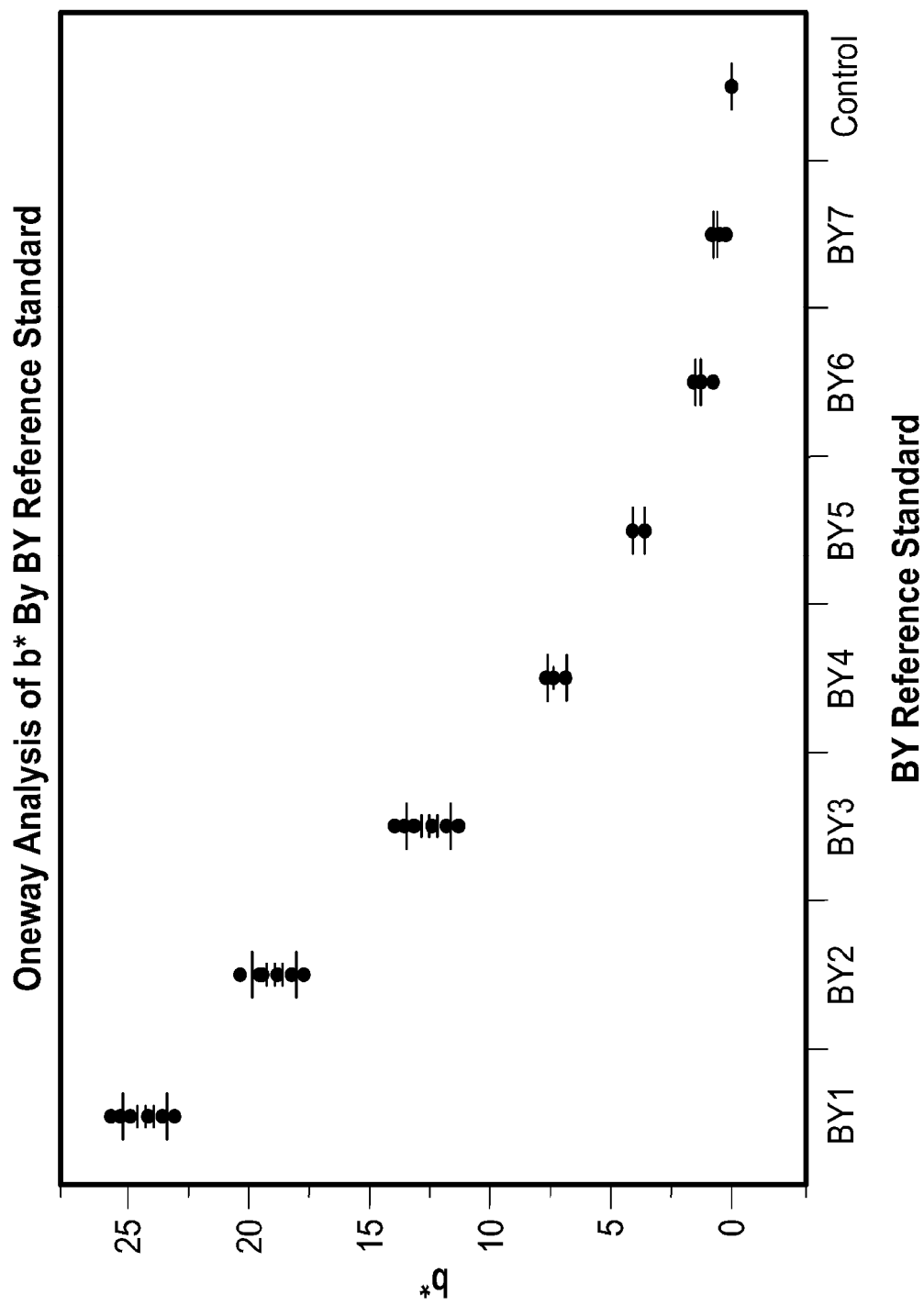


FIG. 9

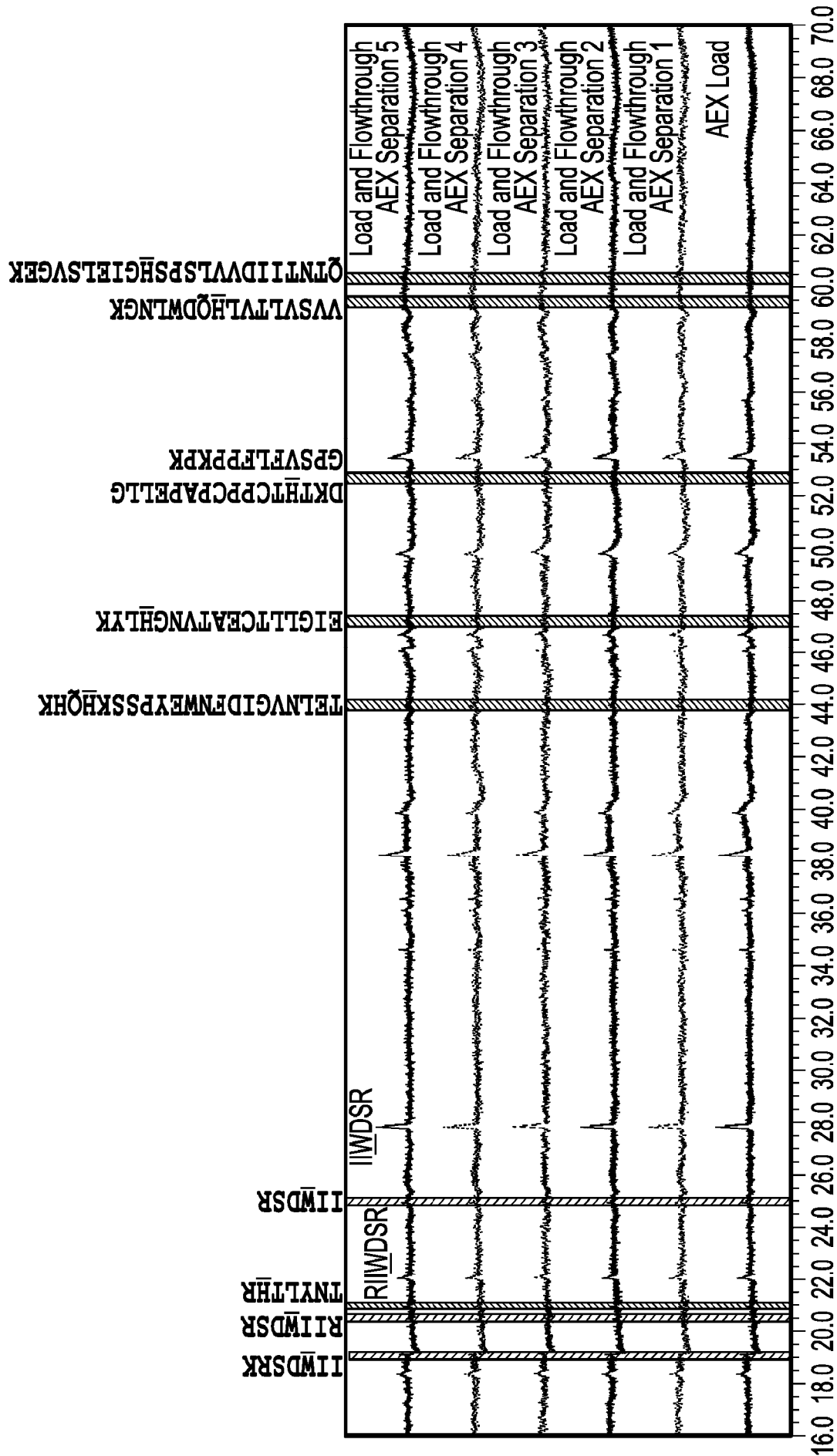


FIG. 10

PTM	Site	Peptide Sequence	Modification	Afibercept AEX Pool					
				Afibercept AEX Load	POROS 50 HQ pH 8.4 2.0 mS/cm	QsFF pH 8.0 2.5 mS/cm	POROS 50 HQ pH 8.0 2.5 mS/cm	QsFF pH 7.8 4.0 mS/cm	POROS 50 HQ pH 7.8 4.0 mS/cm
His Oxidation					AEX Separation 1	AEX Separation 2	AEX Separation 3	AEX Separation 4	AEX Separation 5
				3.06	1.05	0.96	1.33	1.35	1.55
	H19	SDTGRPFVEMYSEIPEIIH <u>MTEGR</u>	+14	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%
	H86	EIGLLTC*EATVNGHLYK	+14	0.013%	0.006%	0.007%	0.008%	0.009%	0.010%
	H95	TNYL <u>THR</u>	+14	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%
	H110	QTNTIIDVVLSPSHGIELSVGEK	+14	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%
	H145	TELNVGIDFNWEYPSSKHQHK	+14	0.067%	0.039%	0.033%	0.035%	0.038%	0.042%
	H209	TH <u>T</u> C*PPC*PAPELLGGPSVFLFPKP <u>K</u>	+14	0.056%	0.027%	0.037%	0.040%	0.045%	0.048%
Trp Oxidation	H295	VVSVLTVLHQDWLNGK	+14	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%
			+4	0.012%	0.008%	0.007%	0.009%	0.009%	0.011%
	W58	IIW <u>D</u> SR	+16	0.027%	0.017	0.022%	0.021%	0.021%	0.023%
			+32	0.114%	0.102%	0.111%	0.121%	0.114%	0.135%
			+48	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%	<0.01%
			+4	0.069%	0.055%	0.040%	0.036	0.039%	0.038%
	W138	TELNVGIDFNWEY <u>P</u> SSK	+16	0.131%	0.078%	0.070%	0.089	0.077%	0.081%
			+32	0.086%	0.057%	0.040%	0.059%	0.046%	0.068%

*:ALKYLATED CYSTEINE

FIG. 11

Full View

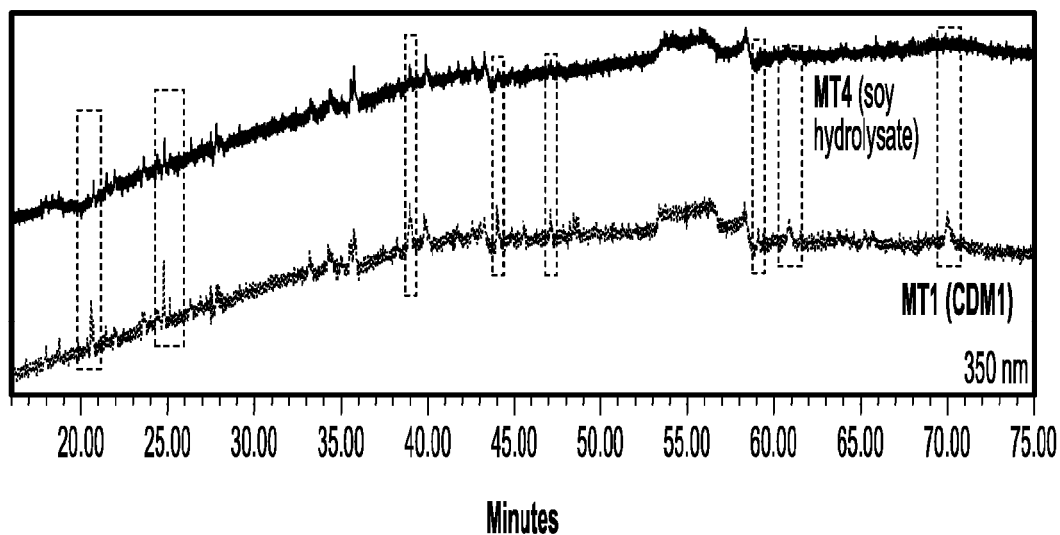


FIG. 12A

16-30 min

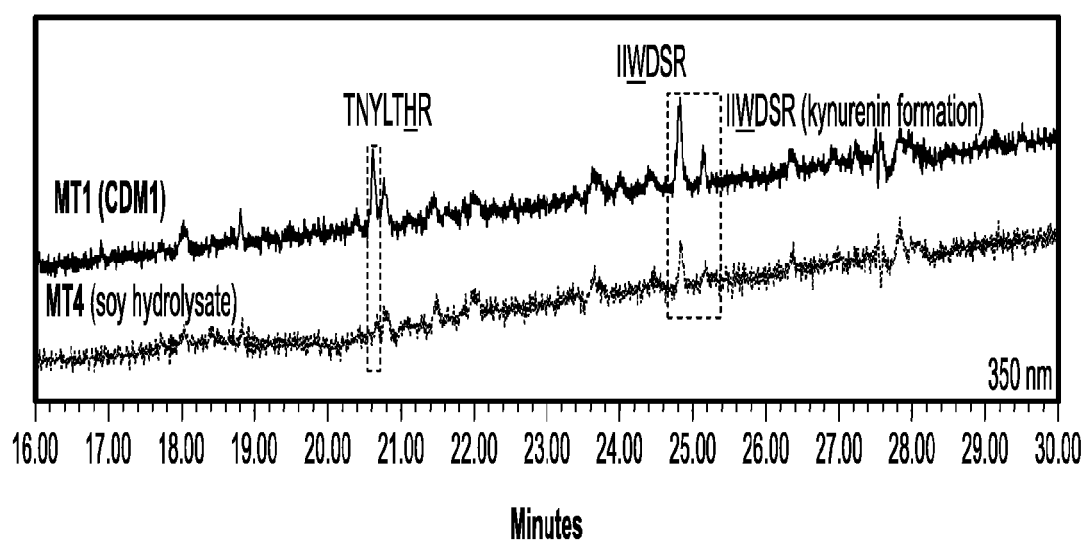


FIG. 12B

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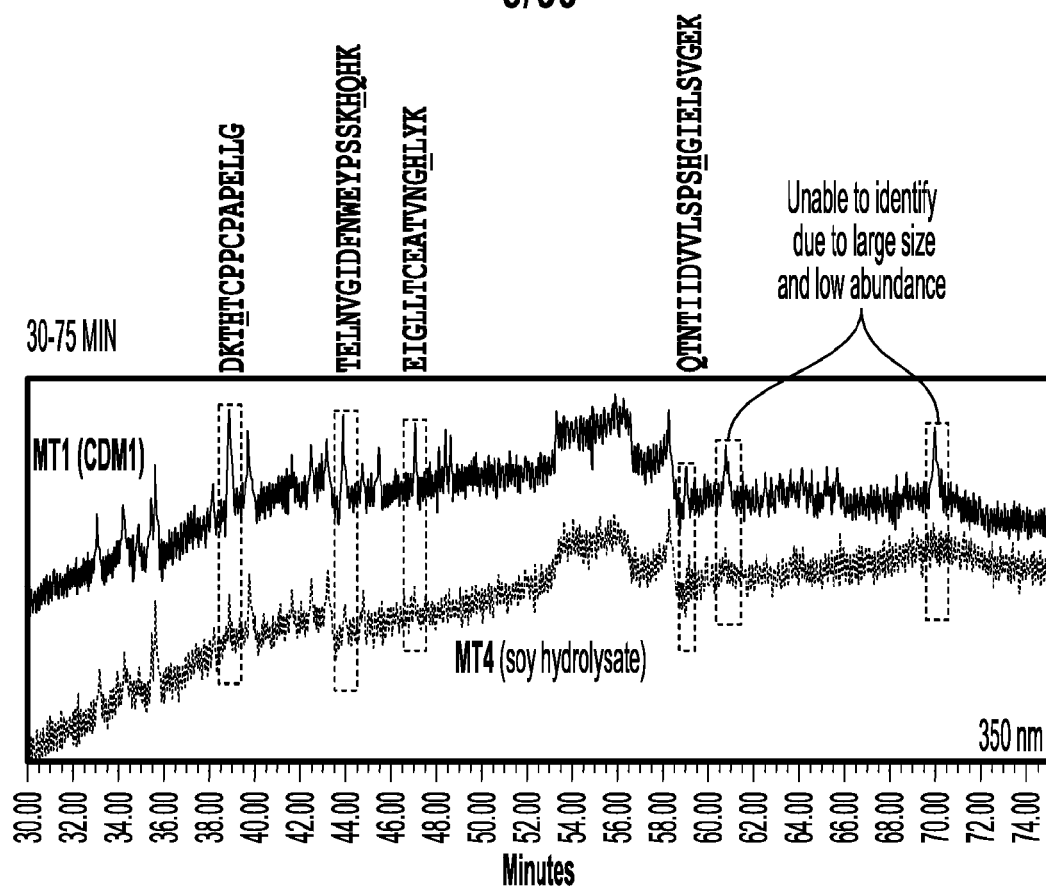


FIG. 12C

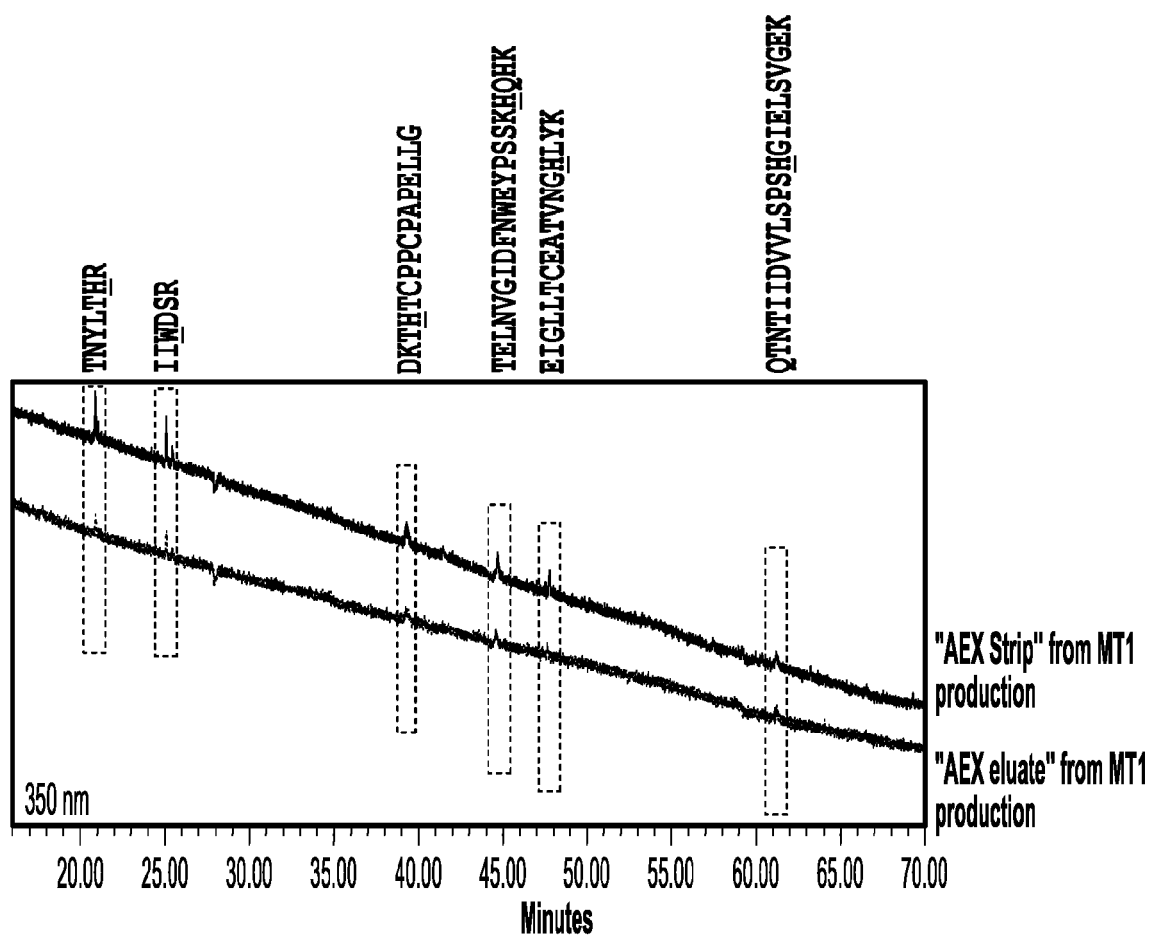


FIG. 13

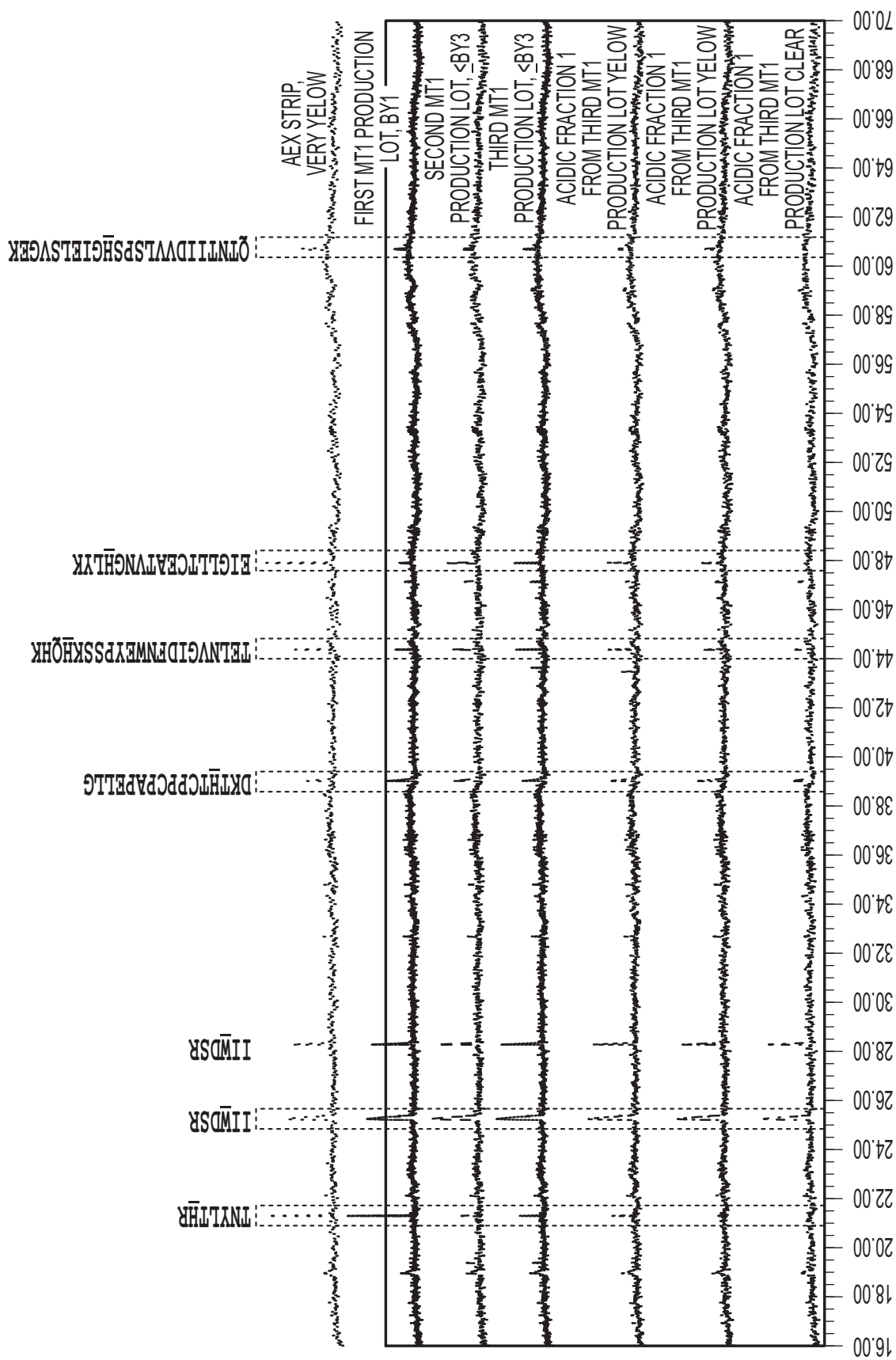


FIG. 14

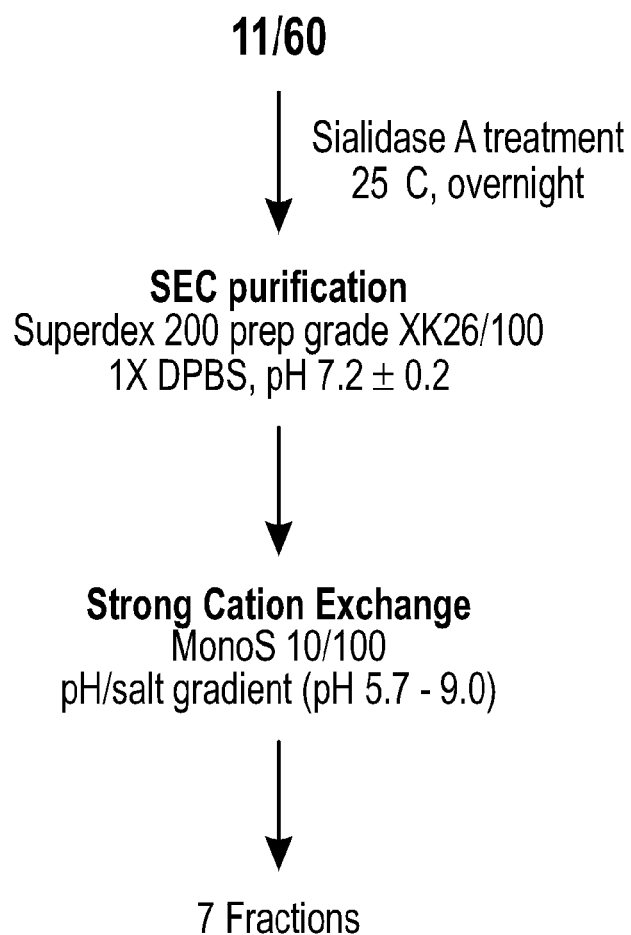


FIG. 15

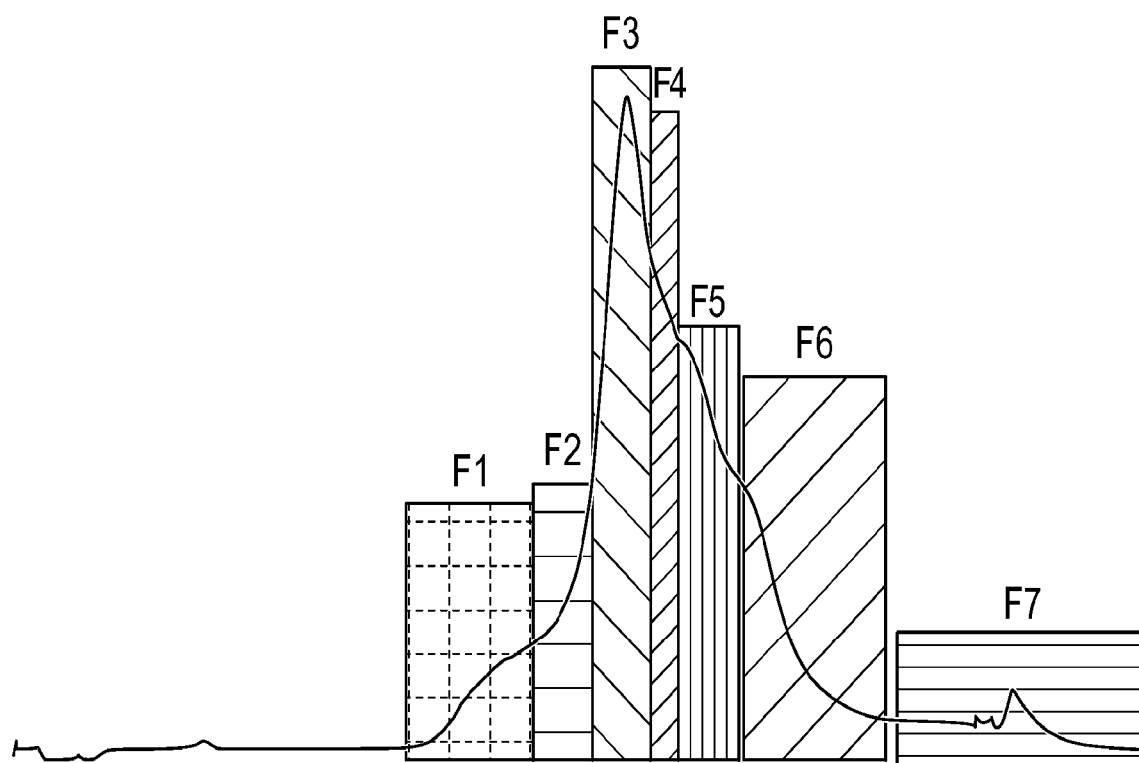


FIG. 16

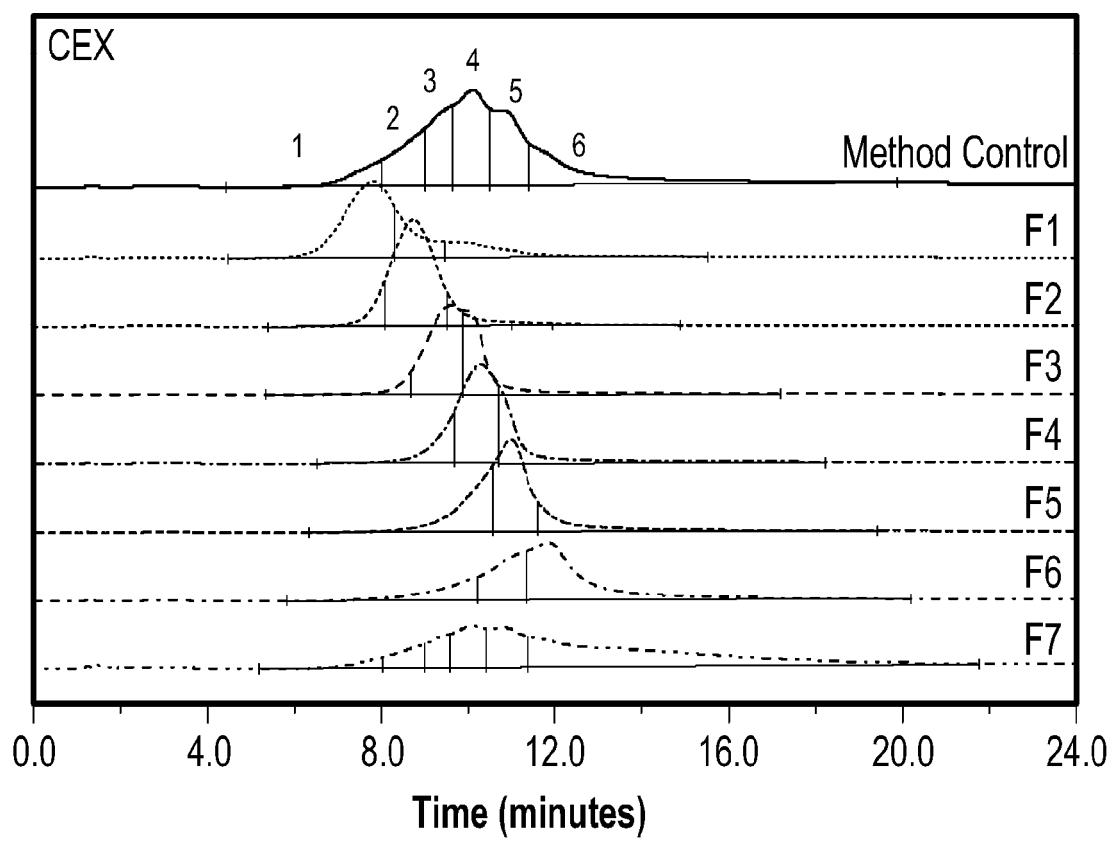


FIG. 17

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MT1 Unfractionated Parental Control

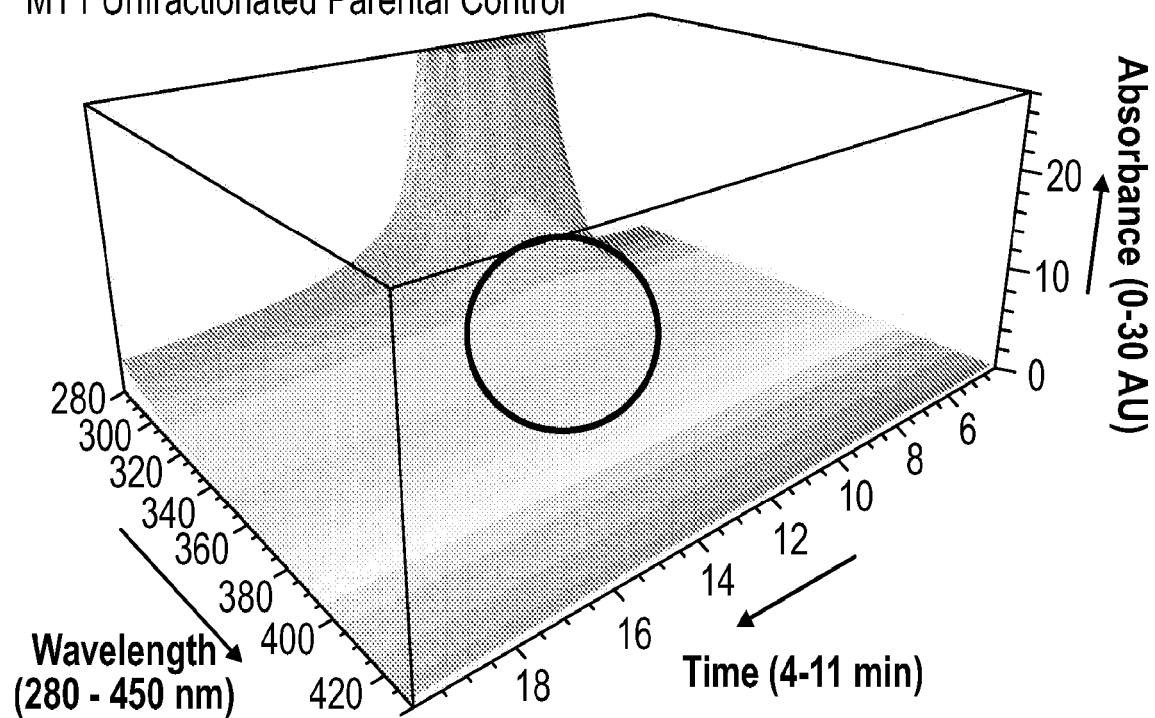


FIG. 18A

MT1 Fraction 1 (F1)

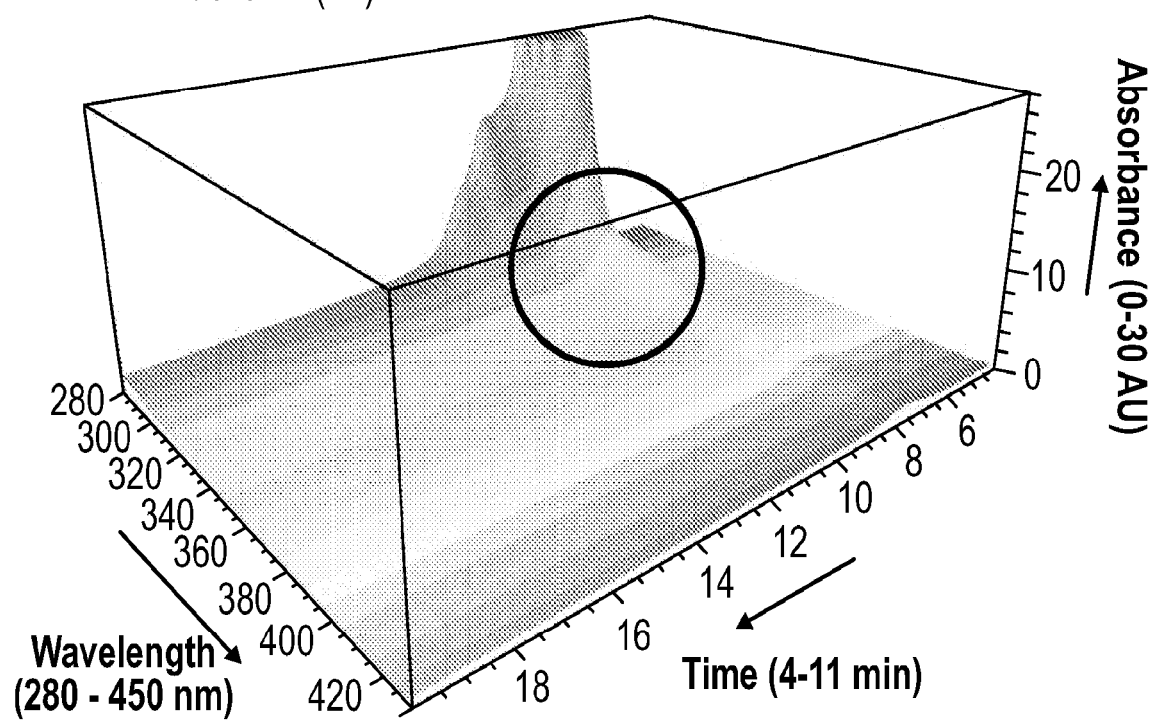


FIG. 18B

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MT1 Fraction 2 (F2)

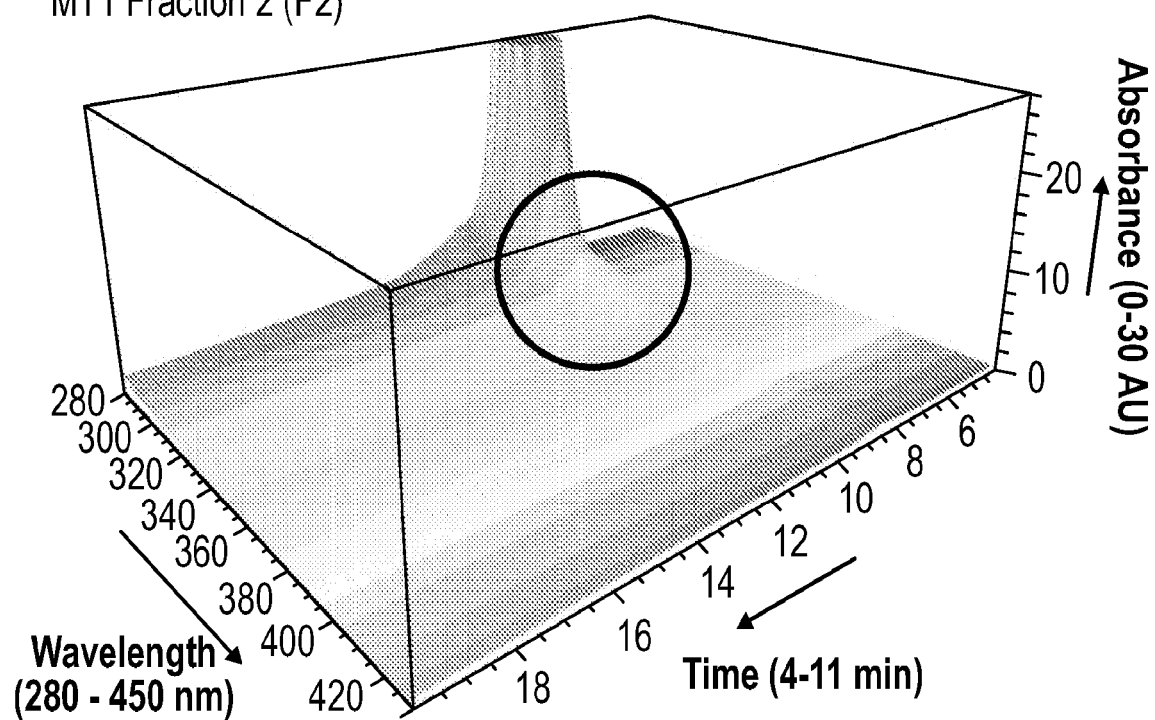


FIG. 18C

MT1 Fraction 3 (F3)

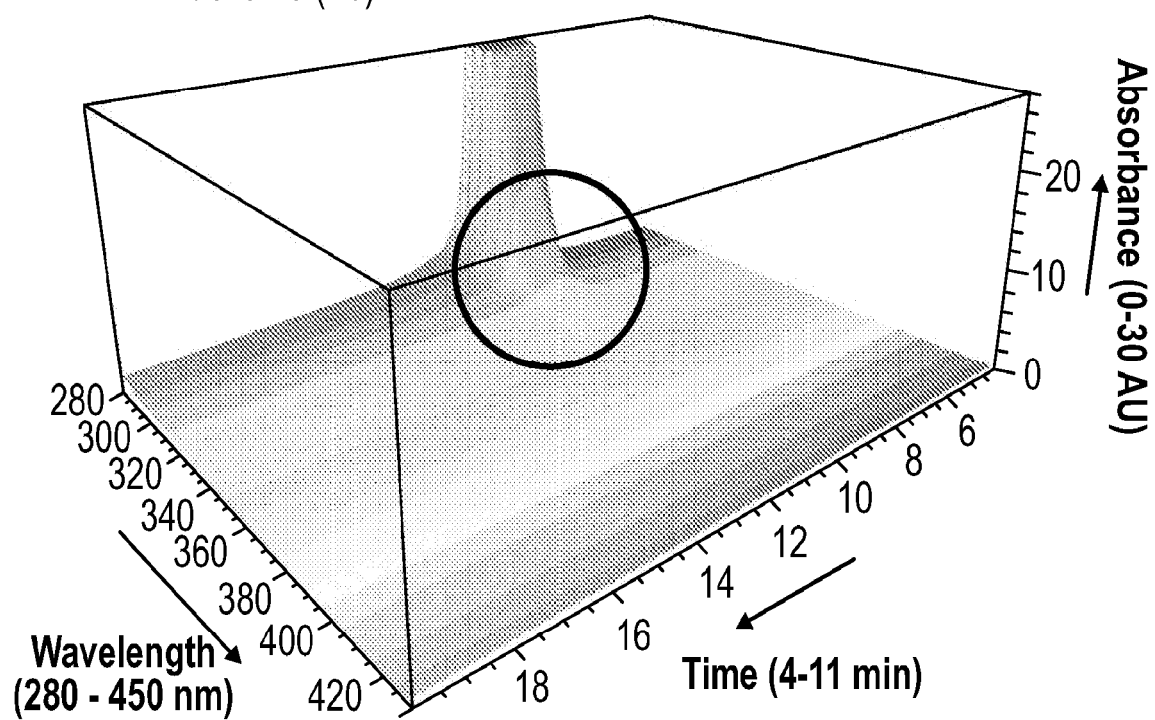


FIG. 18D

MT1 Fraction 4 (F4)

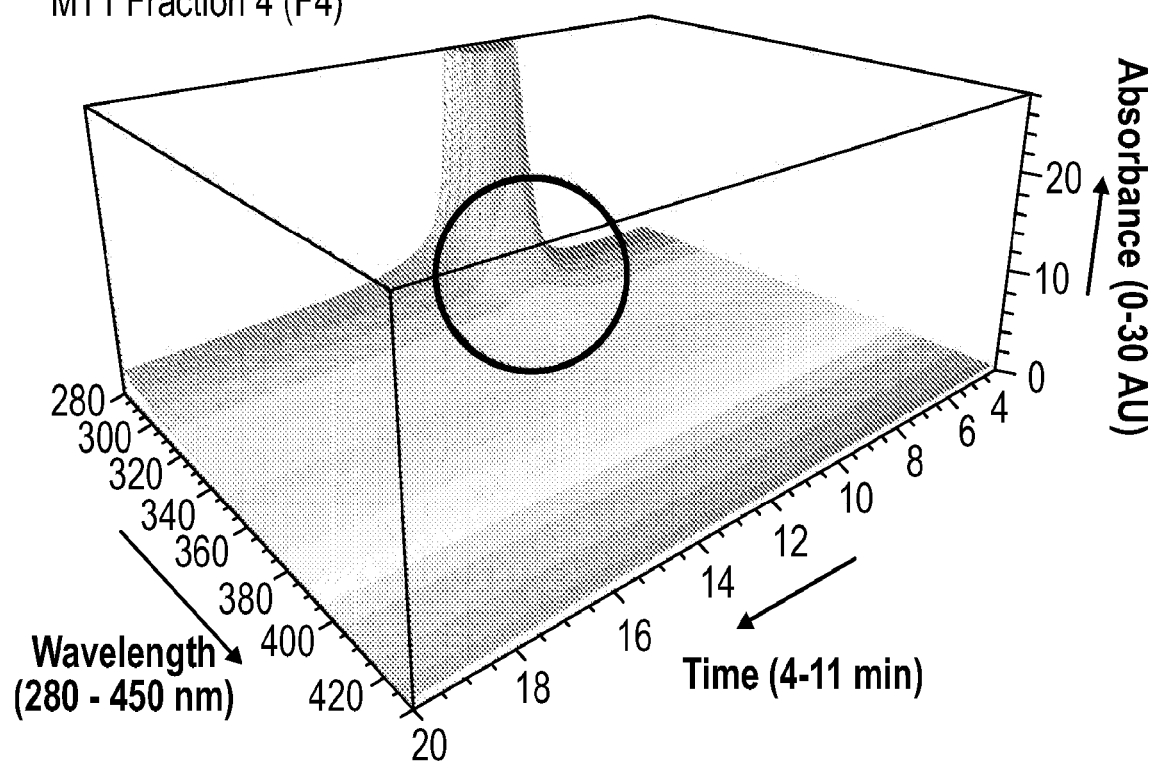


FIG. 18E

MT1 Fraction 5 (F5)

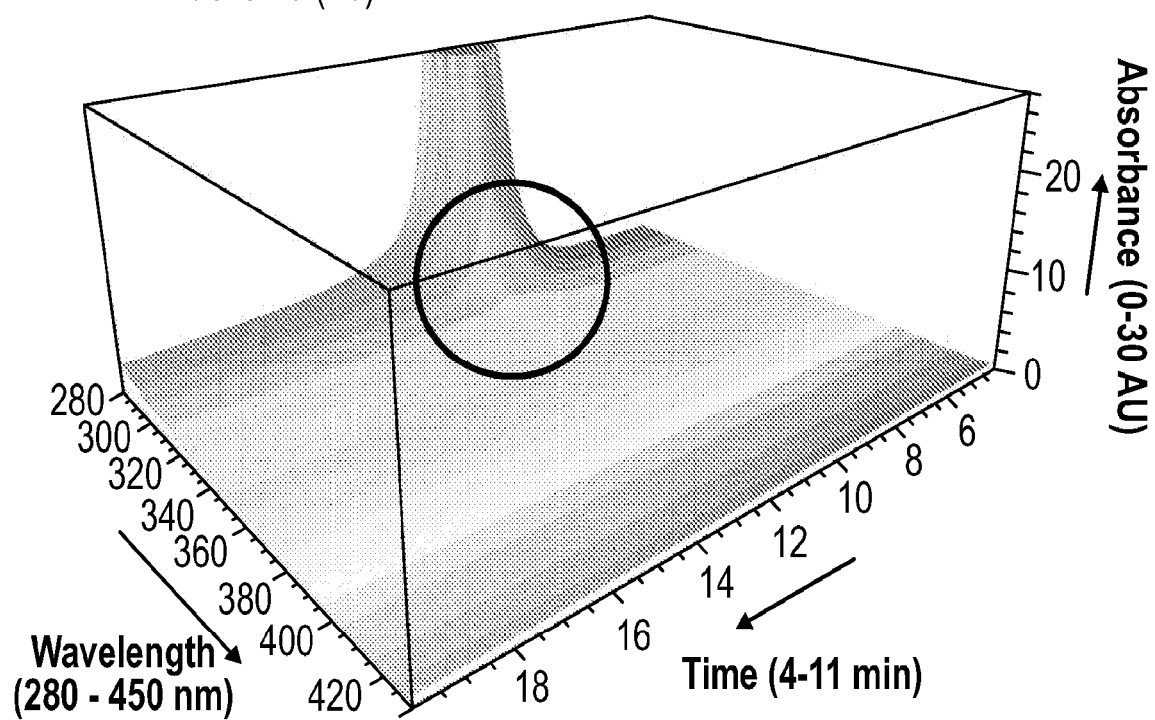


FIG. 18F

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MT1 Fraction 6 (F6)

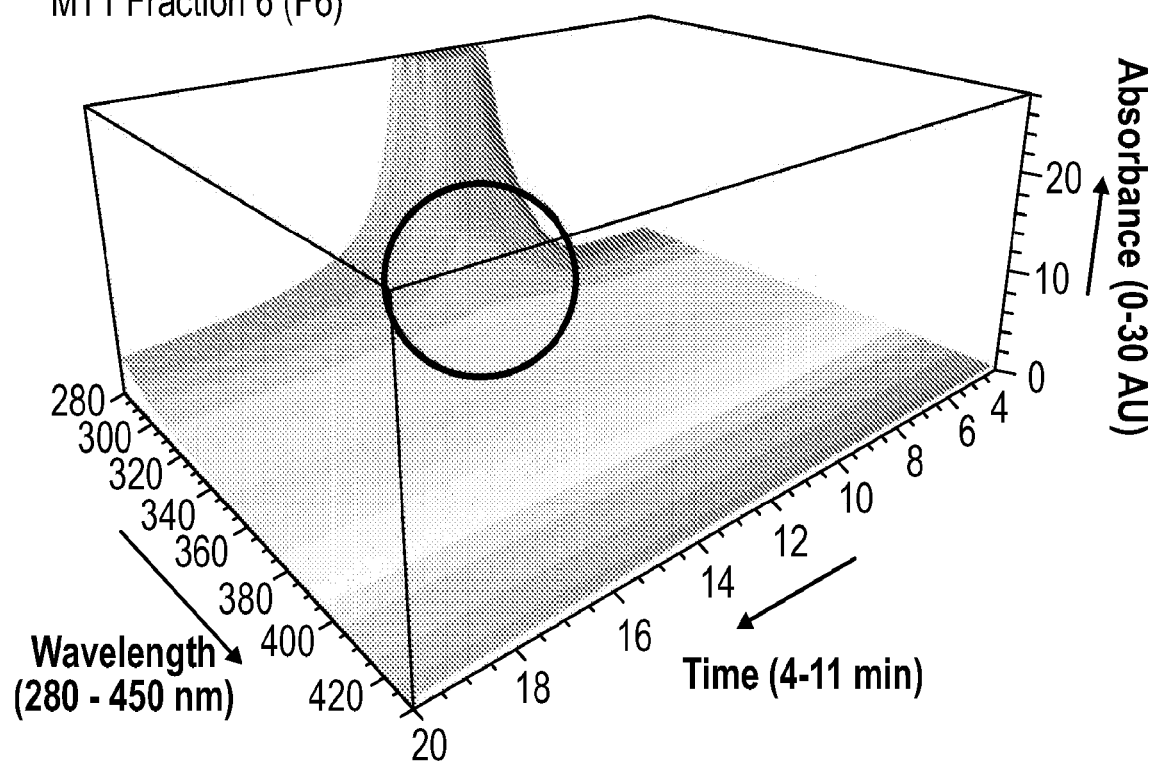


FIG. 18G

MT1 Fraction 7 (F7)

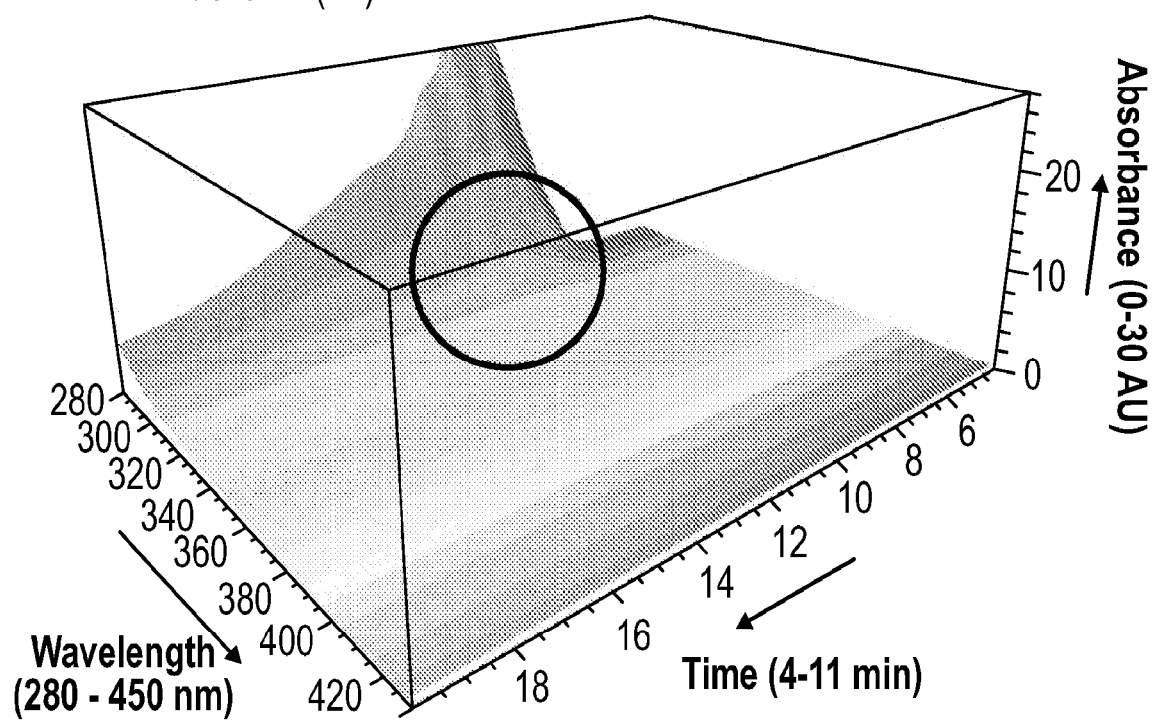


FIG. 18H

iciEF Electropherograms

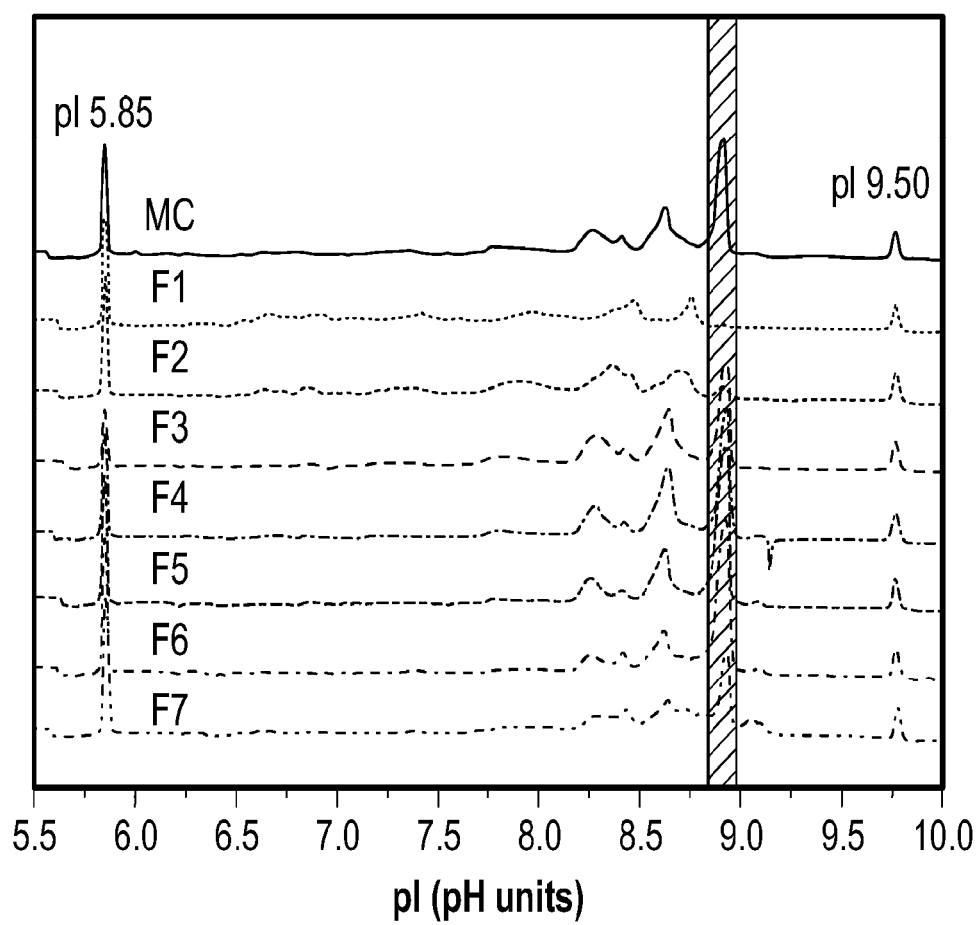
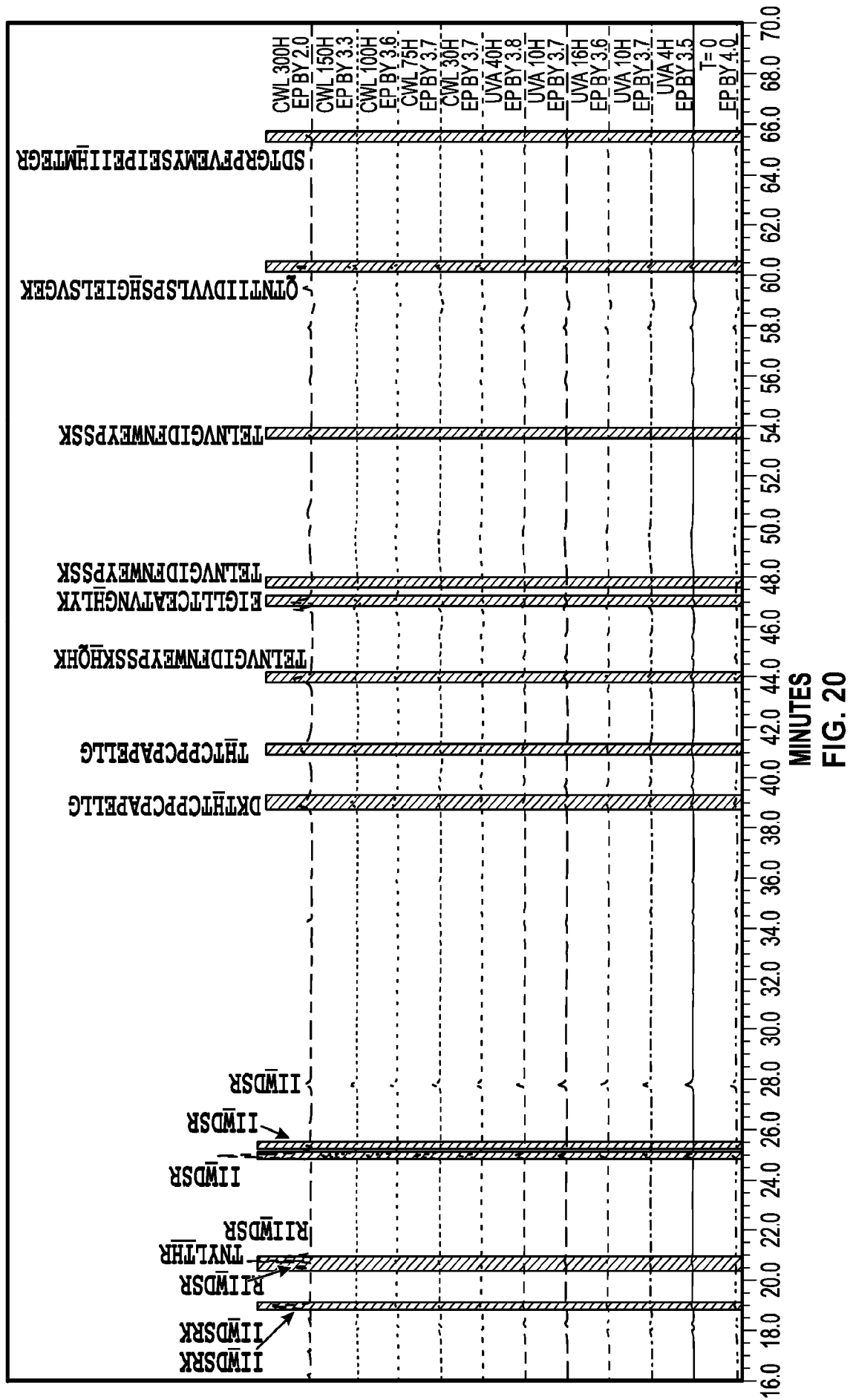


FIG. 19



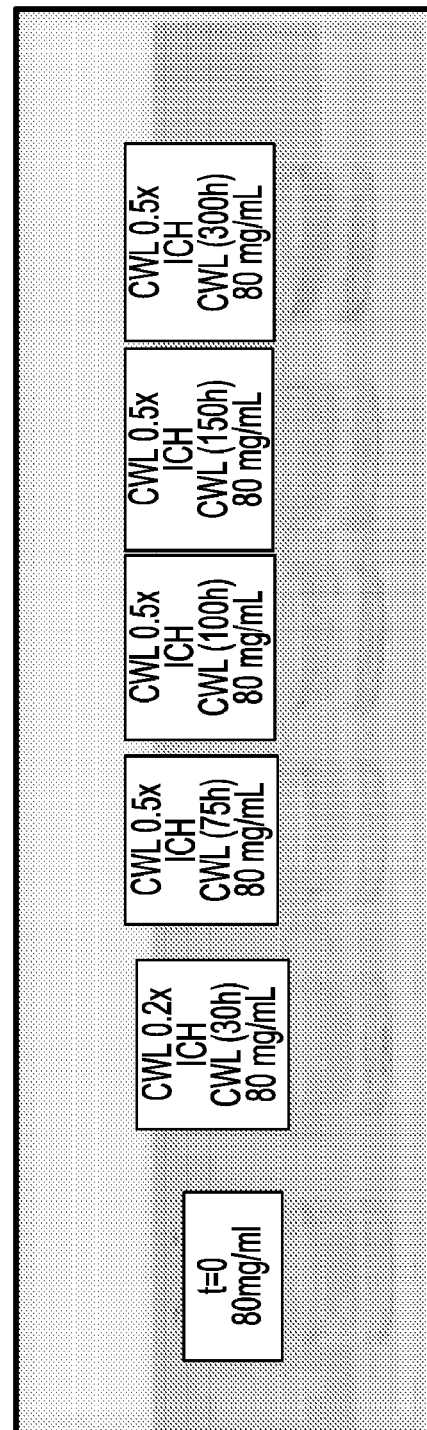
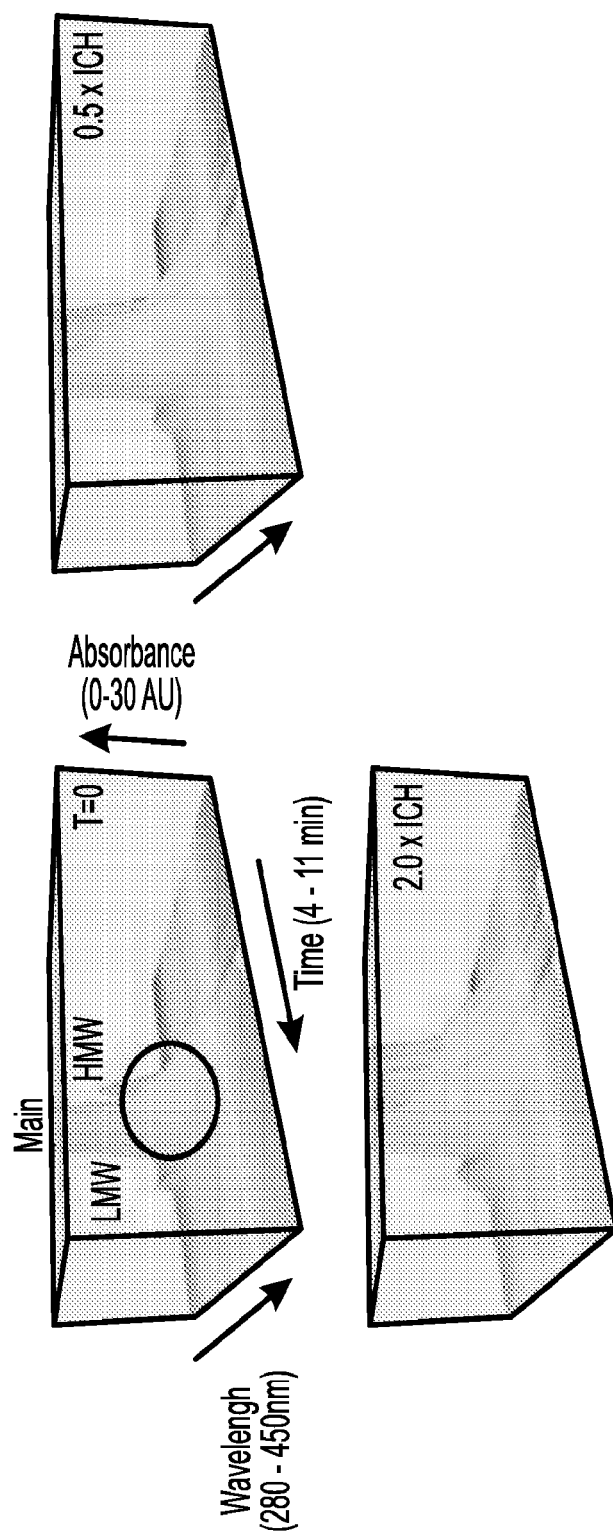


FIG. 21

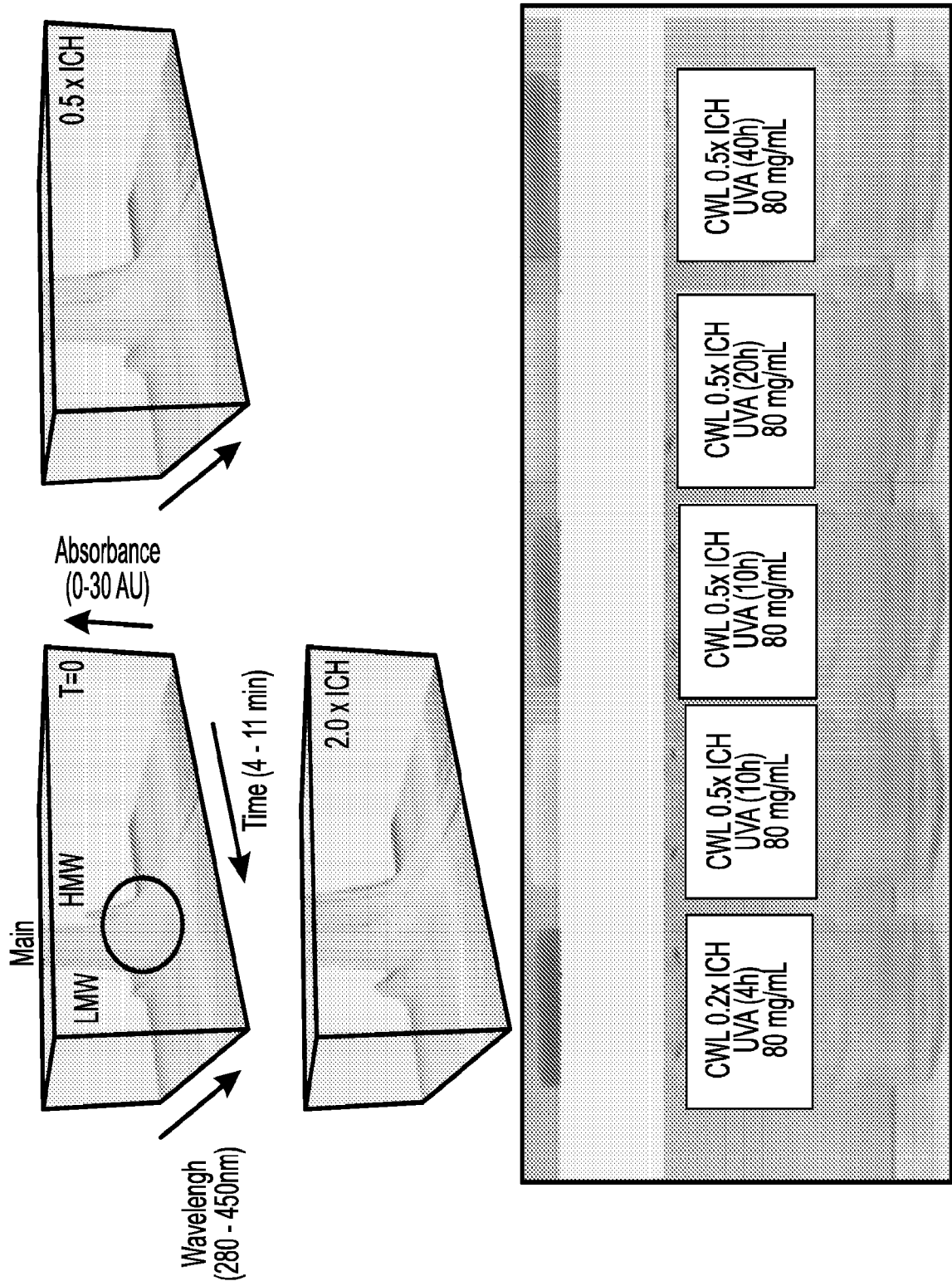


FIG. 22

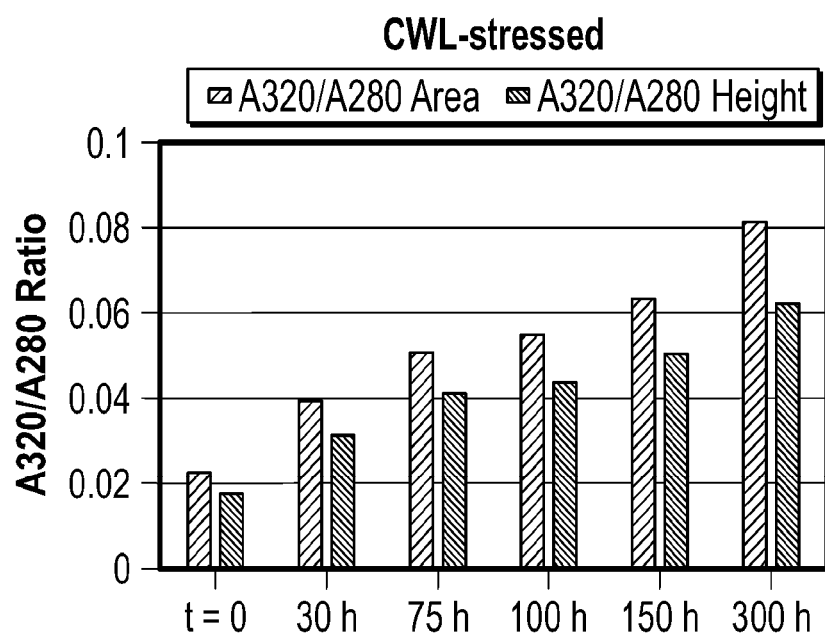


FIG. 23A

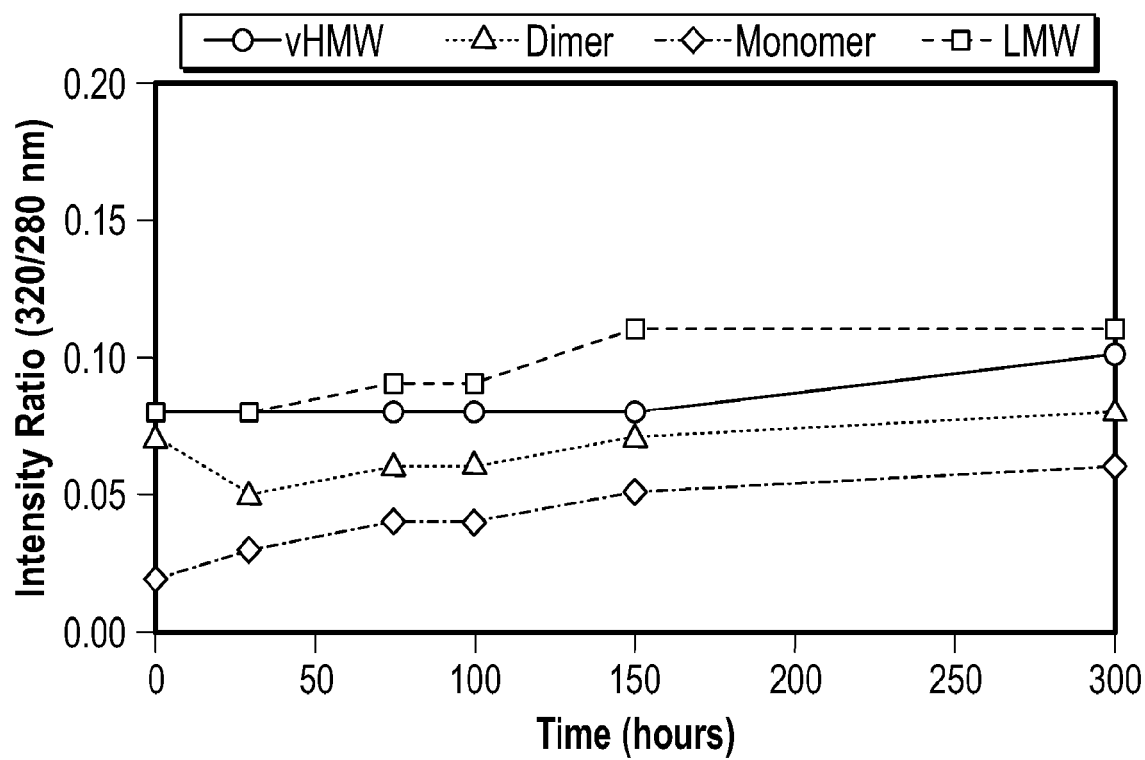


FIG. 23B

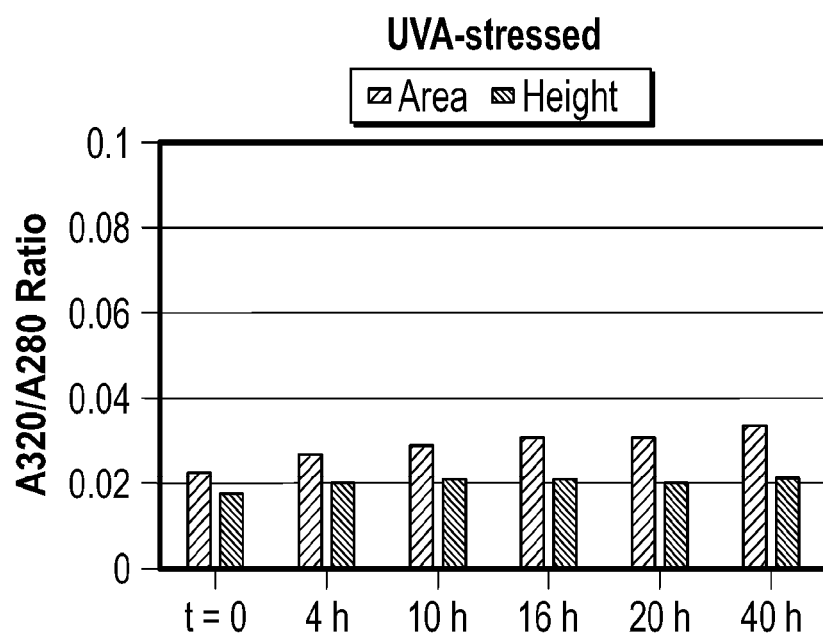


FIG. 24A

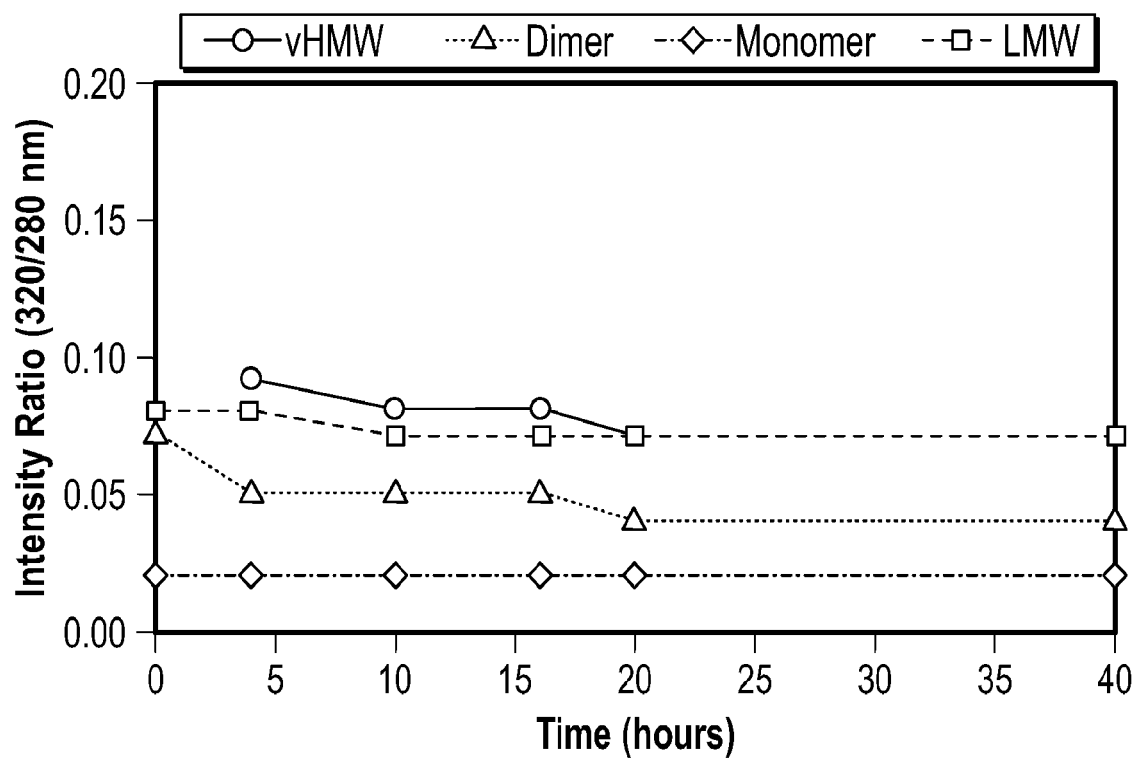


FIG. 24B

Scaled Estimates						
Term	Scaled Estimate			Std Error	t Ratio	Prob> t
Intercept	0.4682071			0.009776	47.89	<.0001*
Cysteine(0,1)	0.3470799			0.009806	35.40	<.0001*
B-Vits Group(0,1)	0.0373611			0.009897	3.78	0.0008*
Iron(0,1)	0.0698208			0.010074	6.93	<.0001*
Zinc(0,1)	0.0538585			0.010255	5.25	<.0001*
Folic Acid(0,1)	0.037899			0.010172	3.73	0.0009*
Cysteine*B-Vits Group	0.0253685			0.009837	2.58	0.0155*
Cysteine*Iron	0.07244			0.01011	7.17	<.0001*
Cysteine*Zinc	0.0339284			0.009973	3.40	0.0020*
Cysteine*Folic Acid	0.0298402			0.010218	2.92	0.0068*
B-Vits Group*Iron	0.0229271			0.009945	2.31	0.0288*
B-Vits Group*Folic Acid	-0.022614			0.010243	-2.21	0.0356*

FIG. 25A

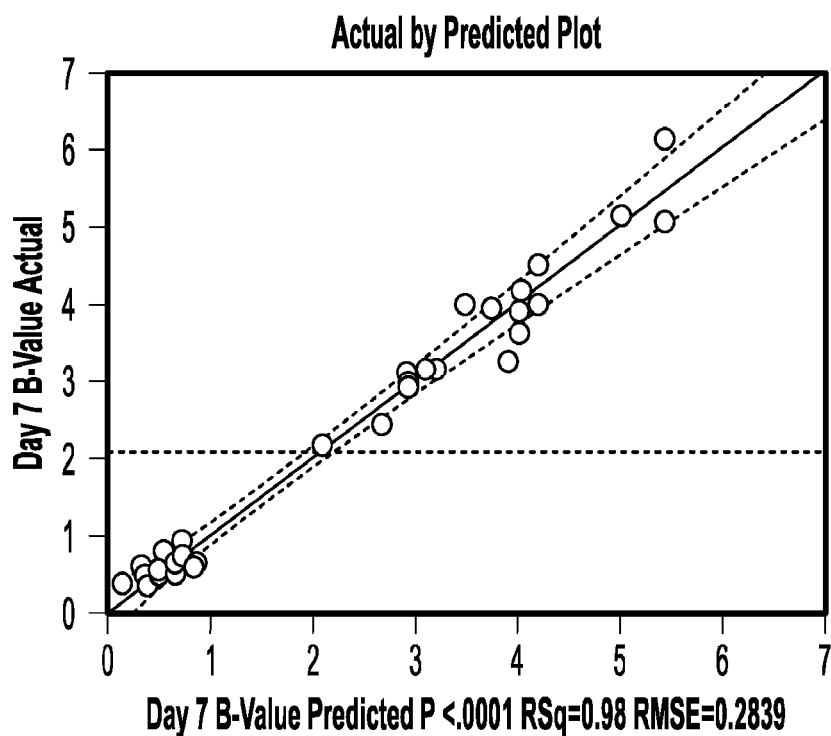


FIG. 25B

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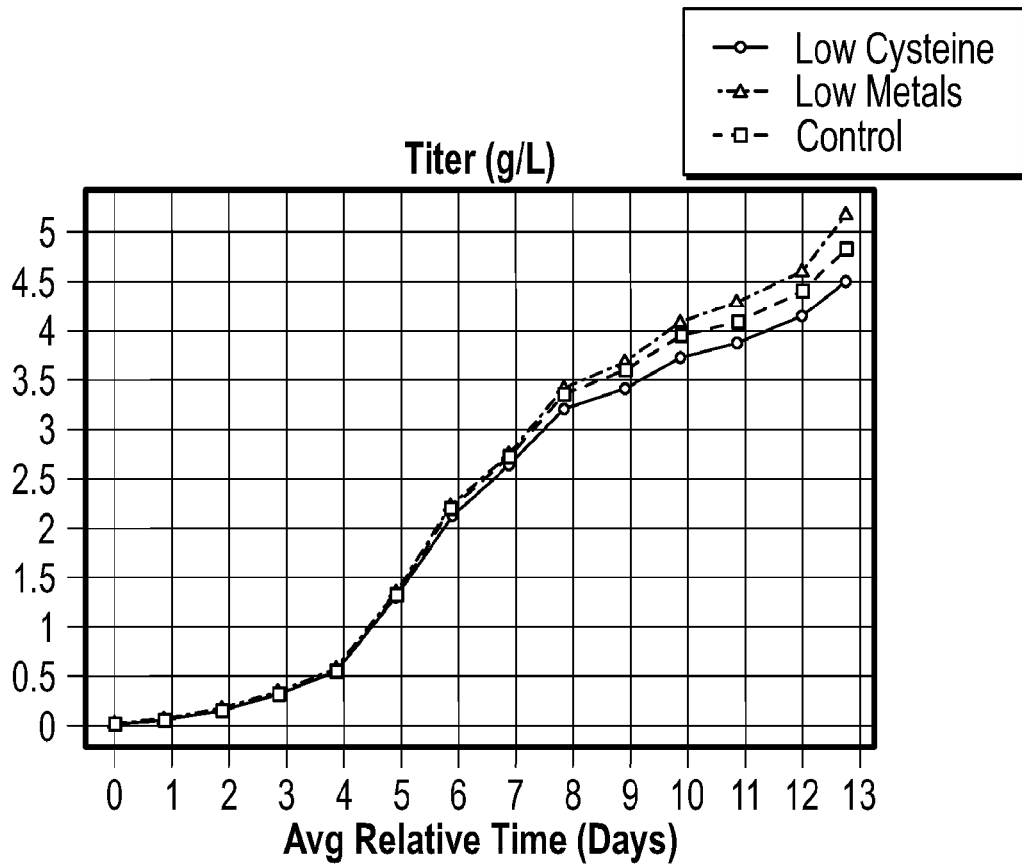


FIG. 26A

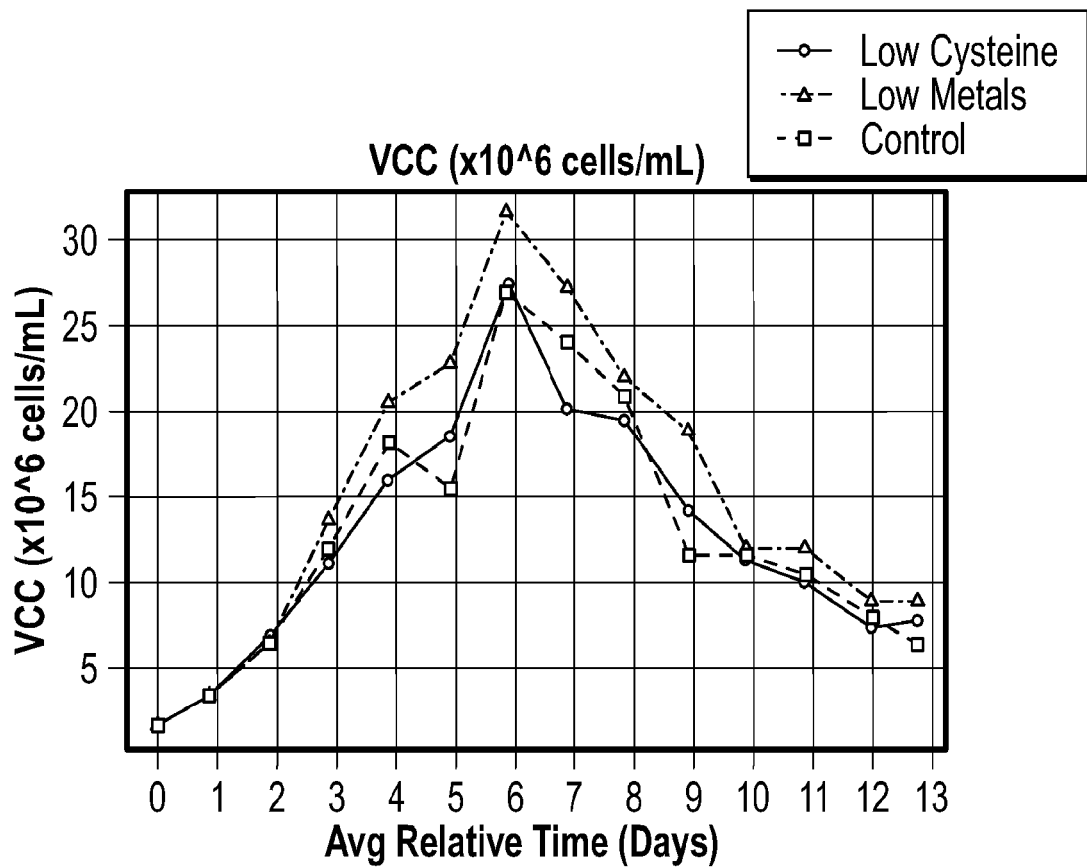


FIG. 26B

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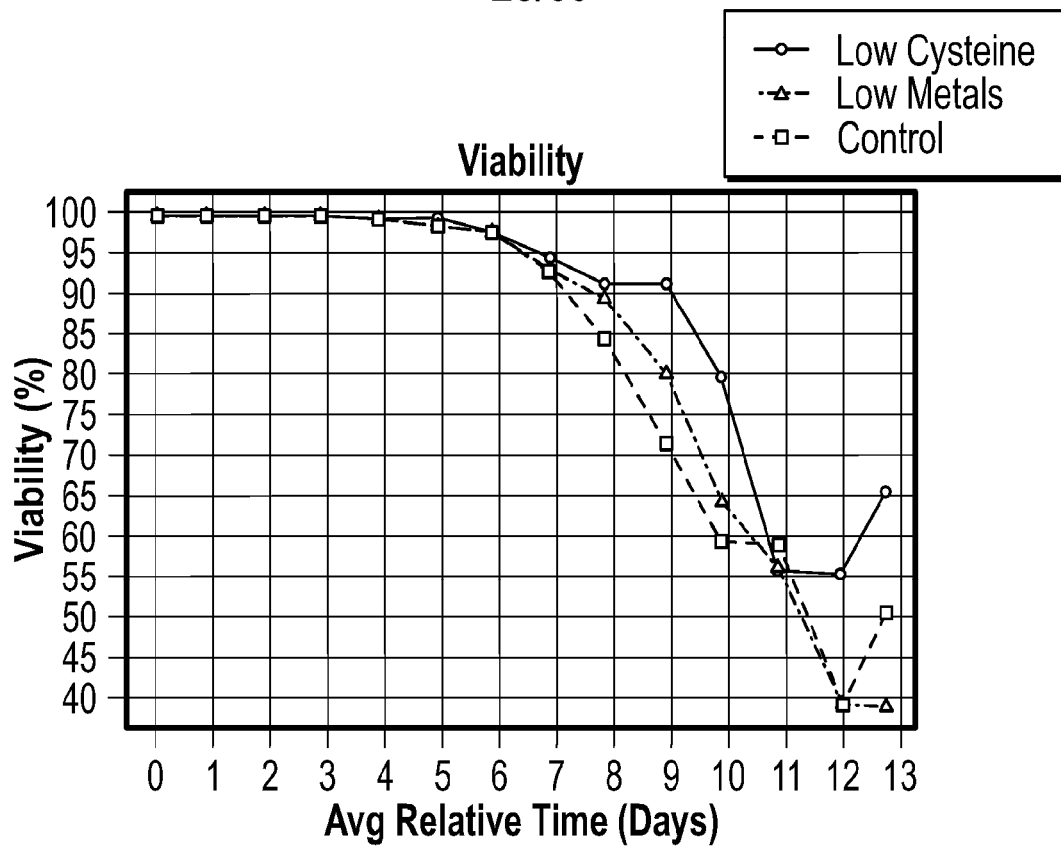


FIG. 26C

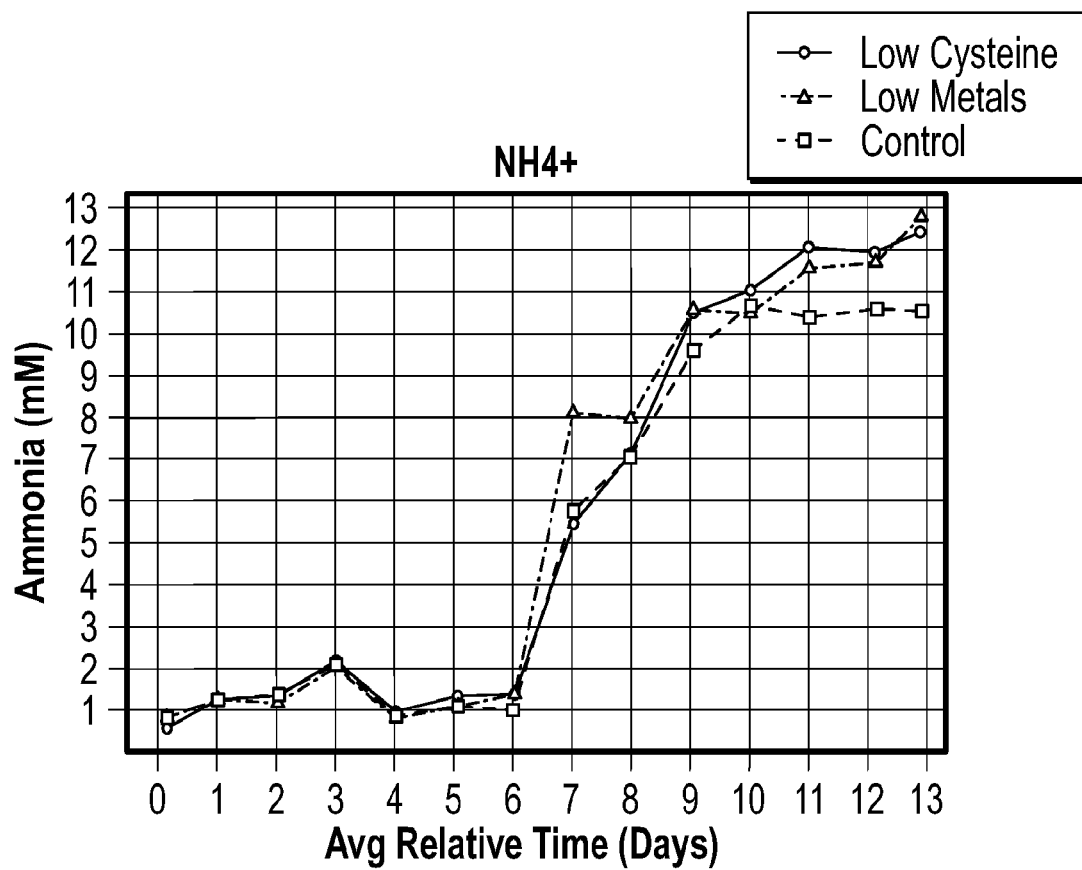


FIG. 26D

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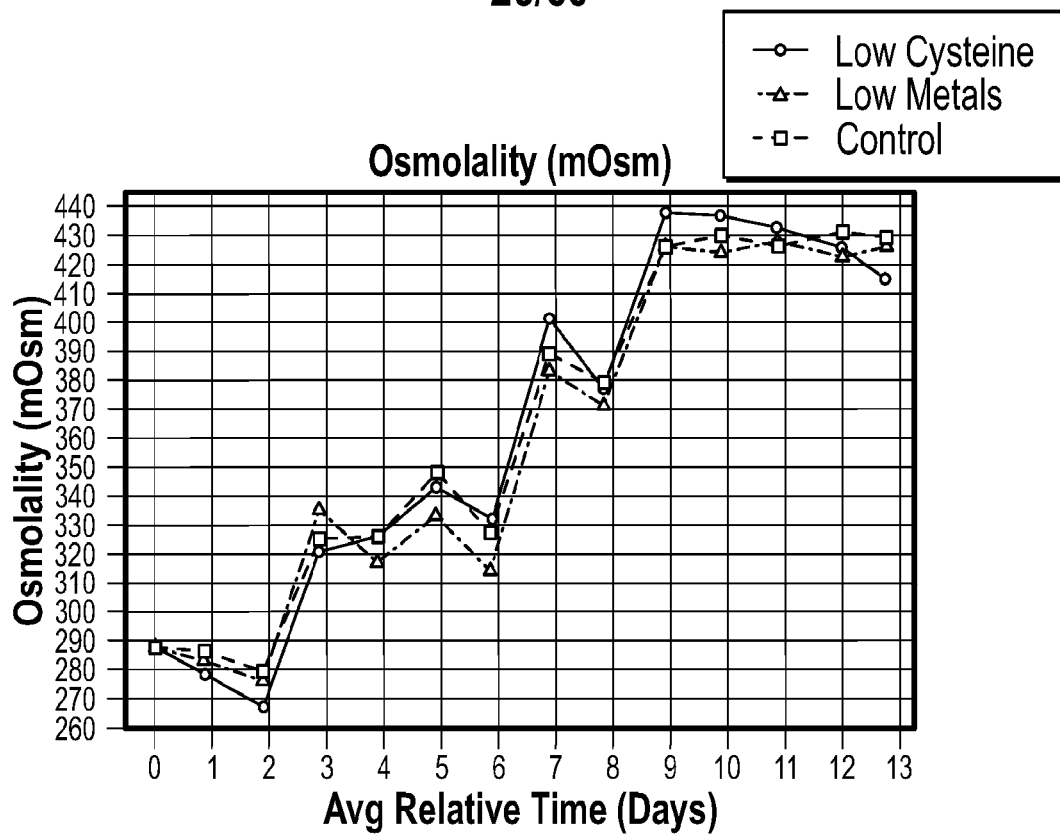


FIG. 26E

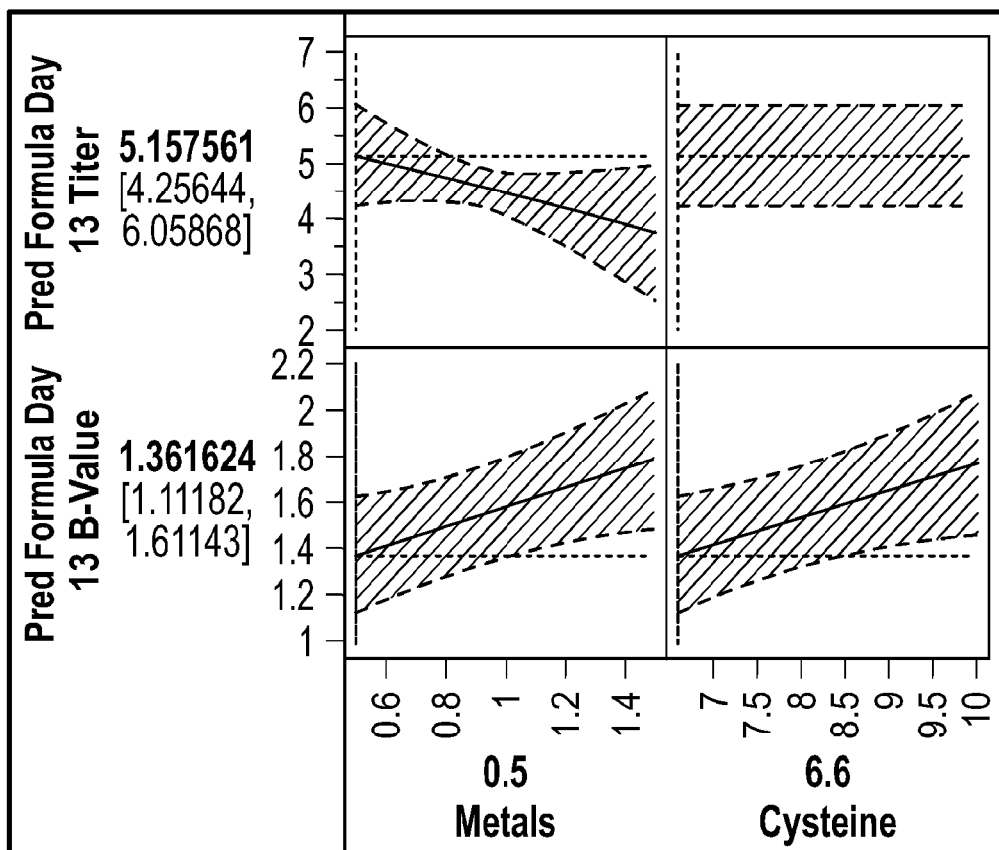


FIG. 27

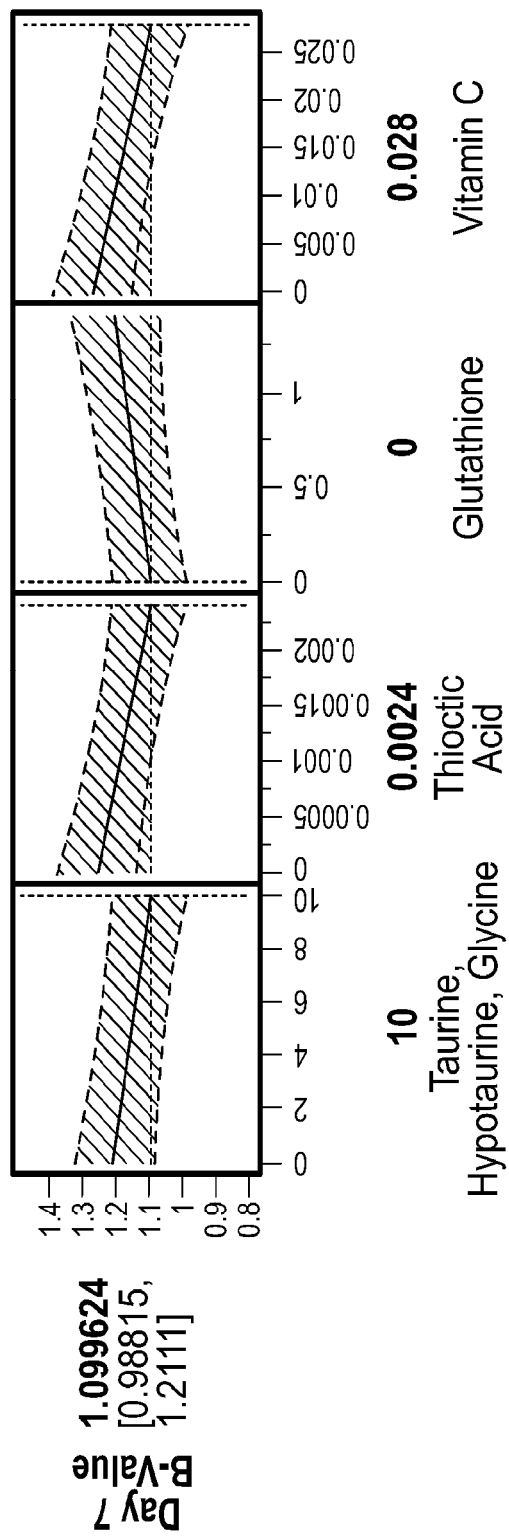


FIG. 28A

Scaled Estimates					
Term	Scaled Estimate	Std Error	t Ratio	Prob> t	
Intercept	1.3997181	0.022019	63.57	<.0001*	
Taurine, Hypotaurine, Glycine(0,1)	-0.153727	0.02201	-6.98	<.0001*	
Thioctic Acid(0,1)	-0.010756	0.022019	-0.49	0.6293	
Glutathione(0,1)	0.152492	0.022112	6.90	<.0001*	
Vitamin C(0,1)	-0.017603	0.02201	-0.80	0.4311	
Taurine, Hypotaurine, Glycine*Glutathione	-0.101323	0.022186	-4.57	0.0001*	
Thioctic Acid*Vitamin C	-0.06684	0.02201	-3.04	0.0054*	

FIG. 28B

Term	Scaled		Std Error	t Ratio	Prob> t
	Estimate				
Intercept	1.079804		0.126434	8.54	0.0010*
Taurine (0,1)	-0.030846		0.040585	-0.76	0.4896
Hypotaurine (0,1)	-0.085952		0.044048	-1.95	0.1228
Glycine (0,1)	-0.181863		0.047269	-3.85	0.0183*
Thioctic Acid (0,1)	0.0575148		0.0465	1.24	0.2838
Vitamin C (0,1)	-0.093266		0.0392	-2.38	0.0761
Taurine*Hypotaurine	0.1943093		0.042535	4.57	0.0103*
Taurine*Thioctic Acid	-0.031889		0.044591	-0.72	0.5140
Taurine*Vitamin C	0.0948234		0.046063	2.06	0.1086
Hypotaurine*Thioctic Acid	-0.009982		0.045049	-0.22	0.8355
Hypotaurine*Vitamin C	0.1509187		0.043708	3.45	0.0260*
Thioctic Acid*Vitamin C	-0.176346		0.043781	-4.03	0.0158*
Taurine*Taurine	0.3679087		0.117837	3.12	0.0355*
Hypotaurine*Hypotaurine	0.192703		0.110017	1.75	0.1547
Glycine*Glycine	-0.270392		0.11851	-2.28	0.0846

FIG. 28C

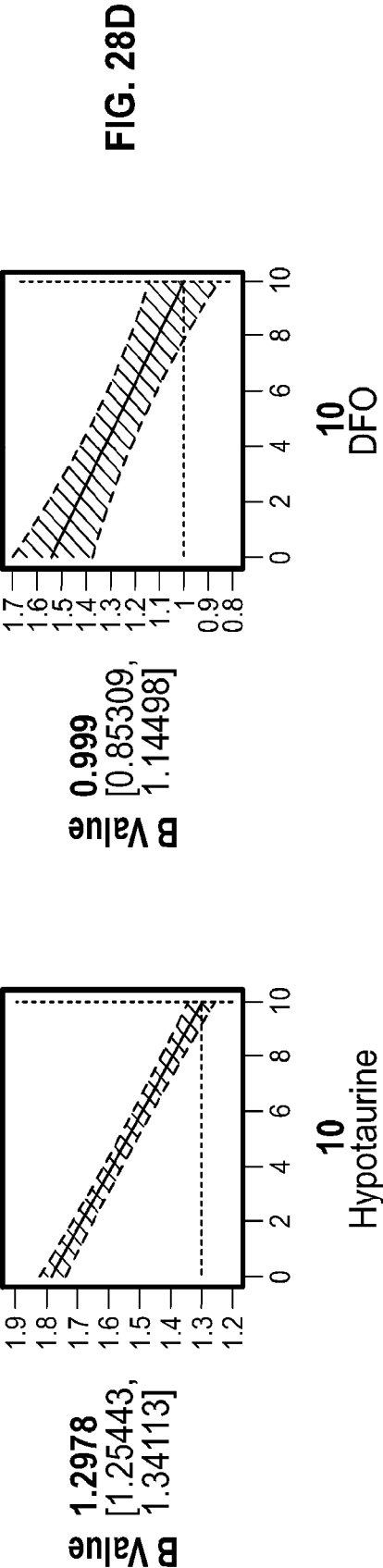


FIG. 28D

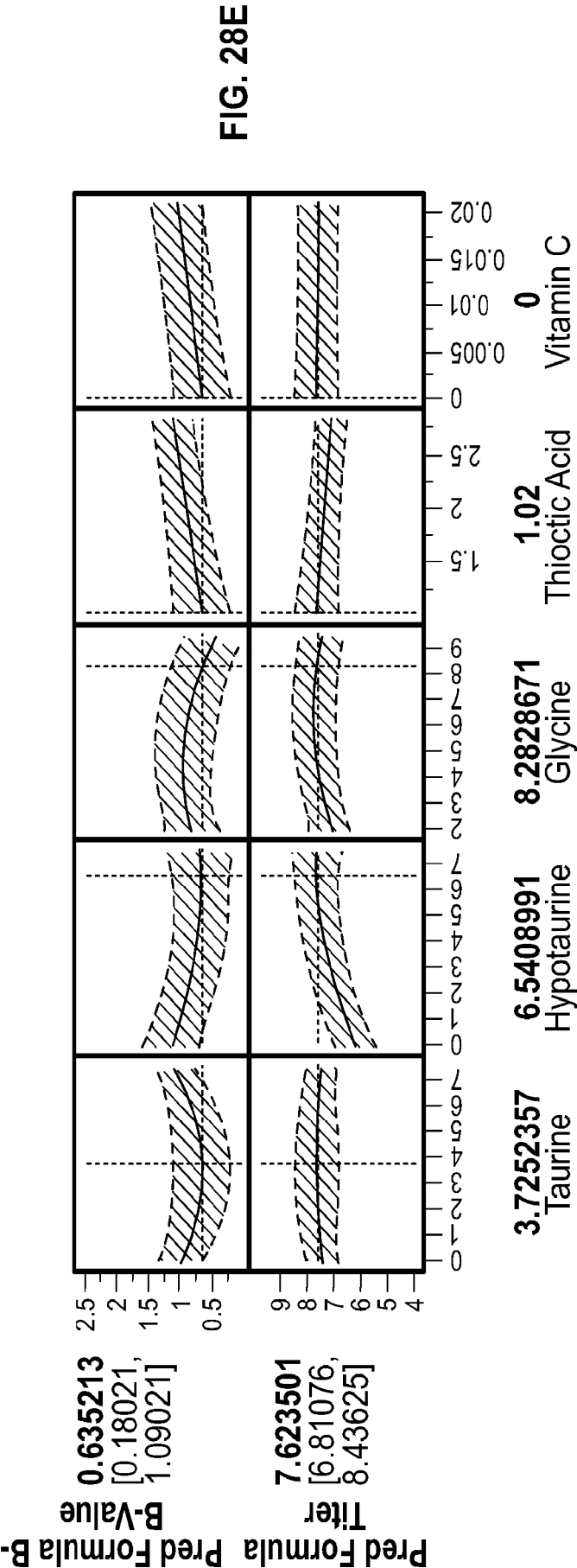


FIG. 28E

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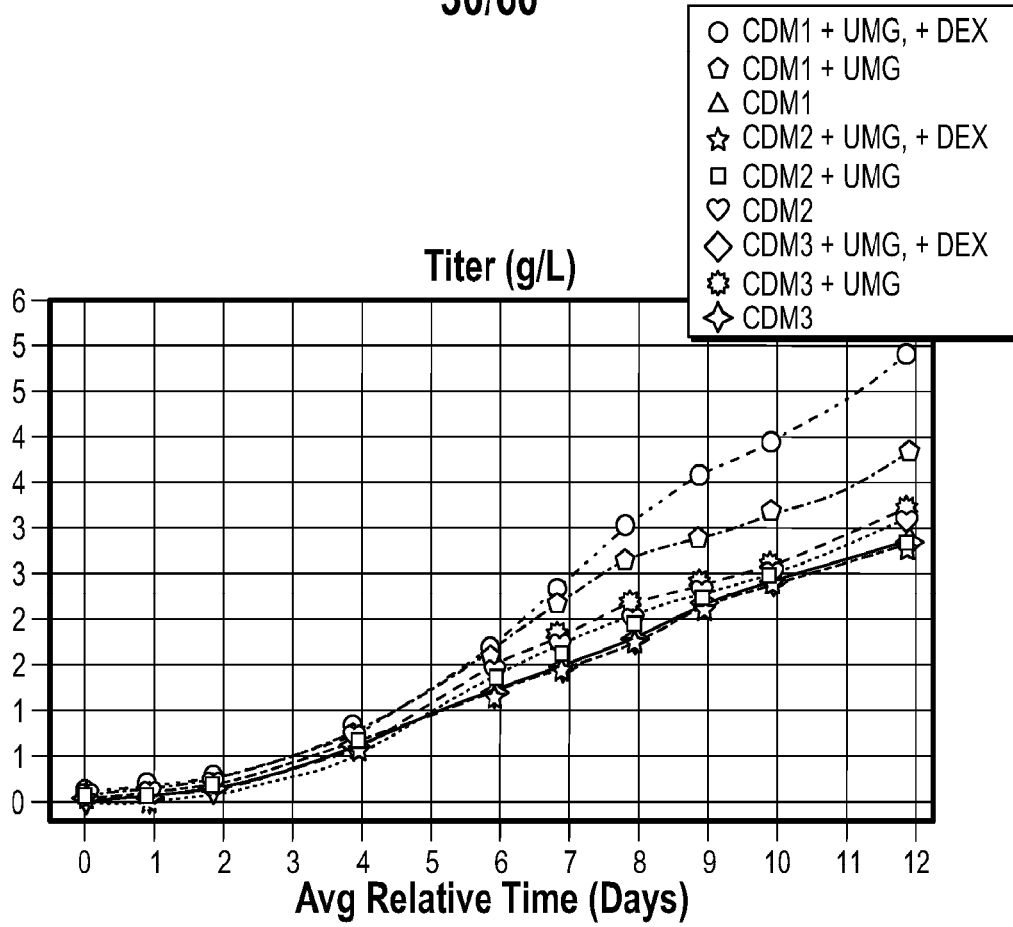


FIG. 29

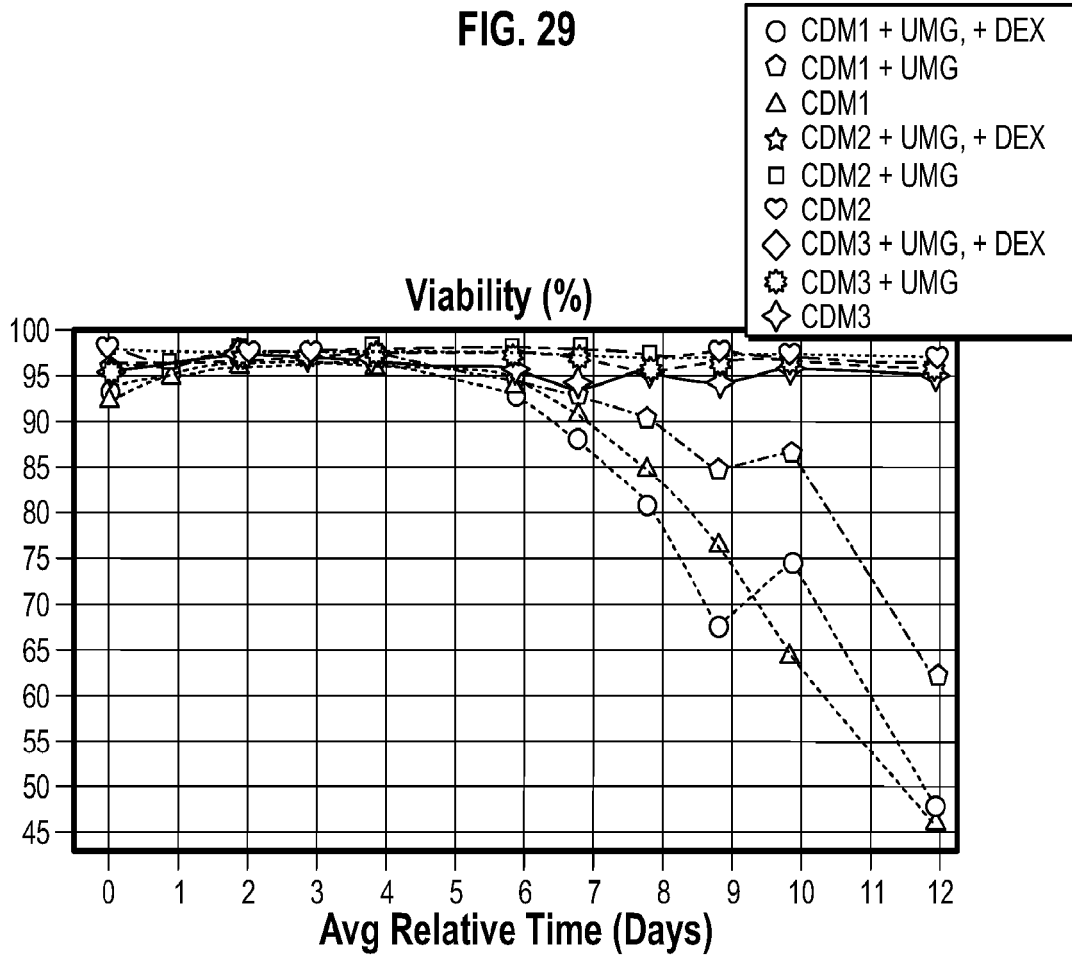
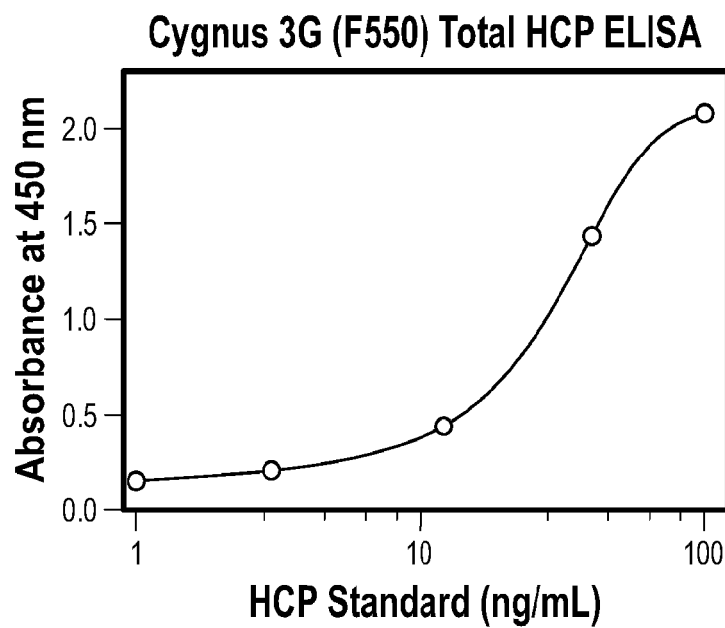
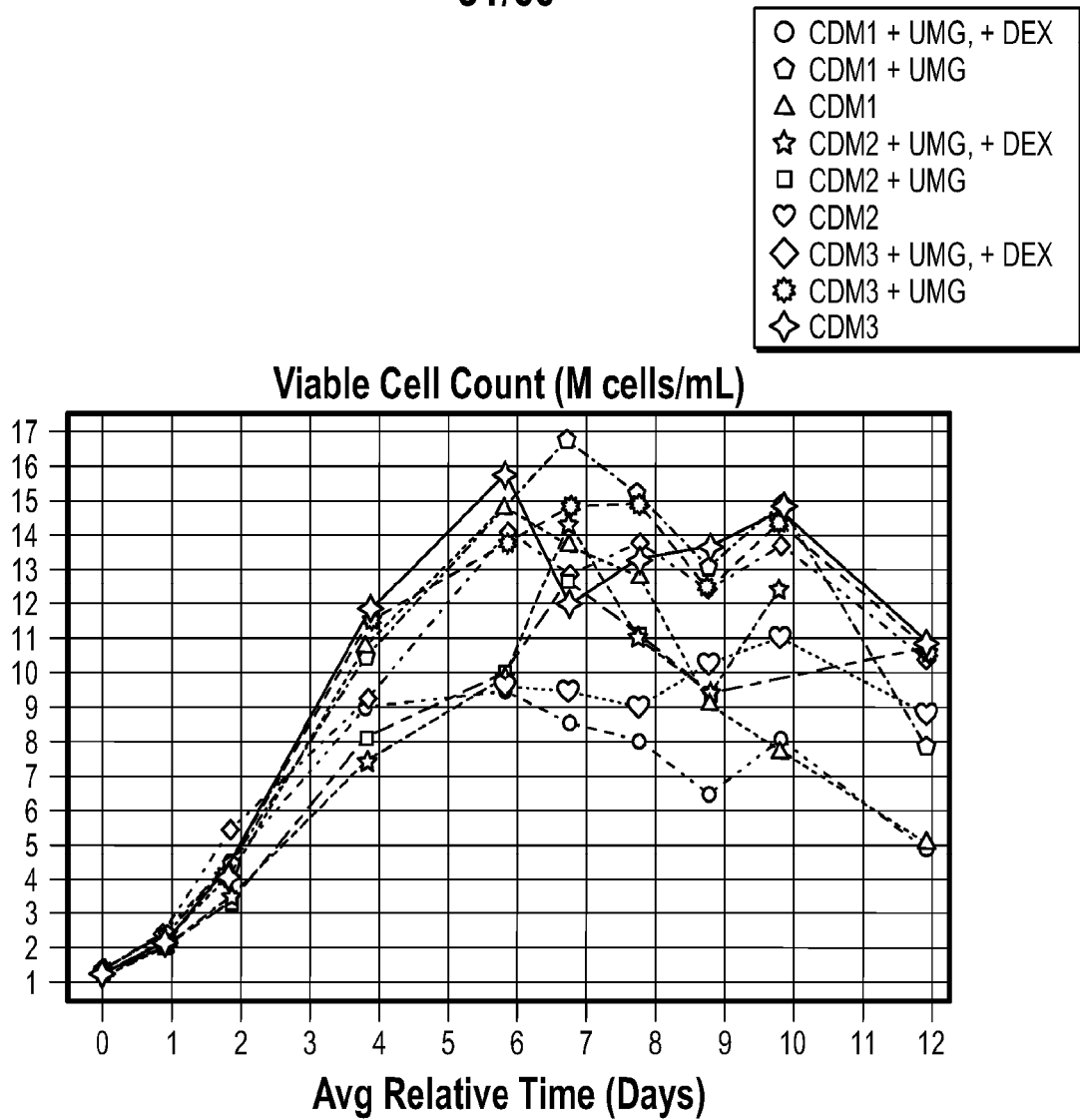


FIG. 30



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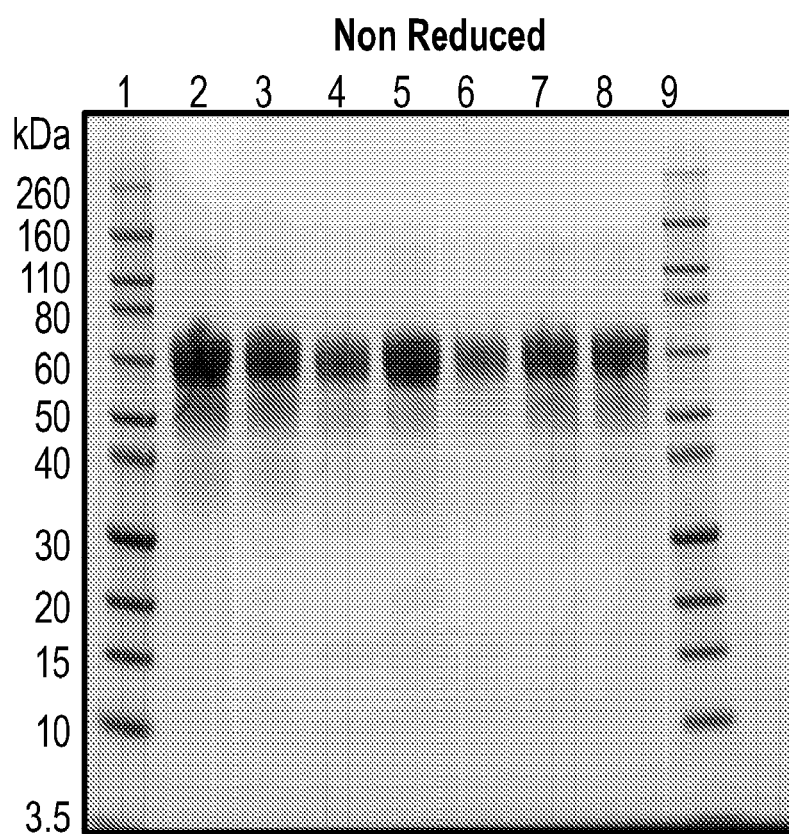


FIG. 33

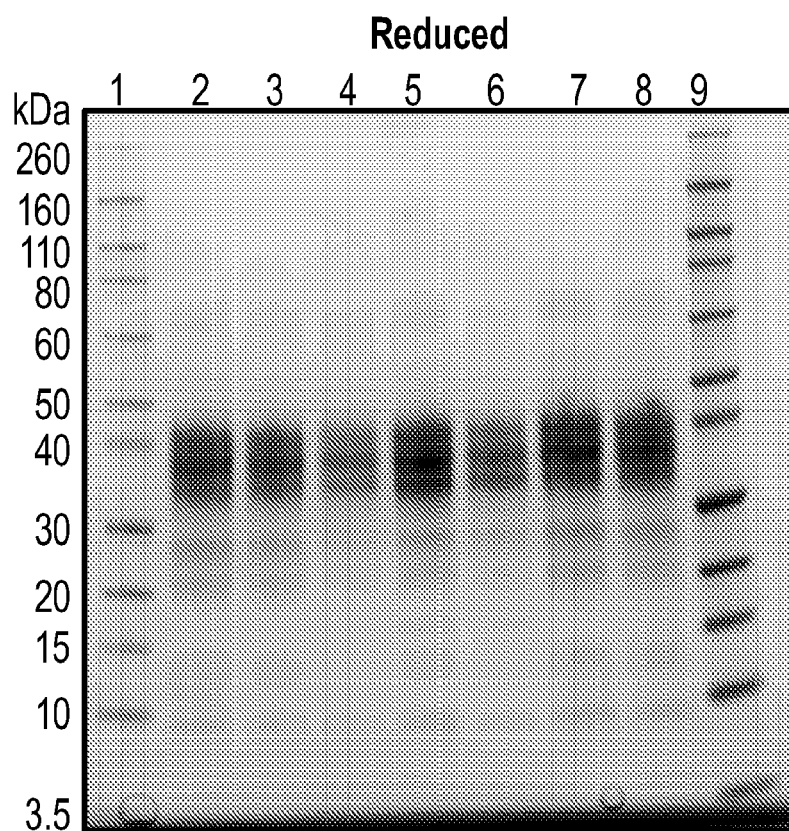


FIG. 34

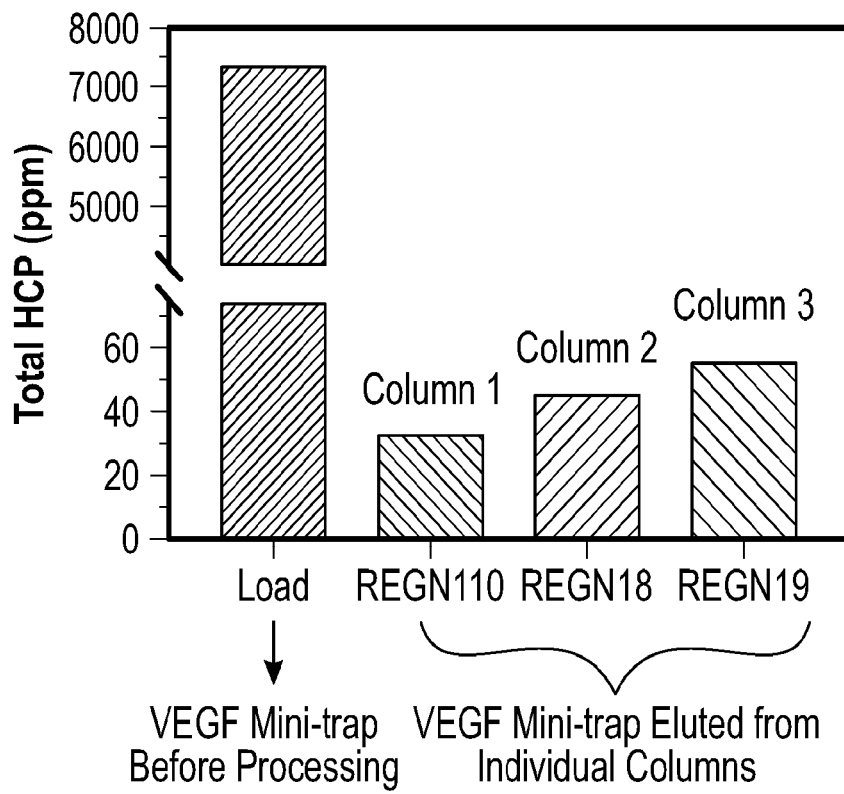


FIG. 35A

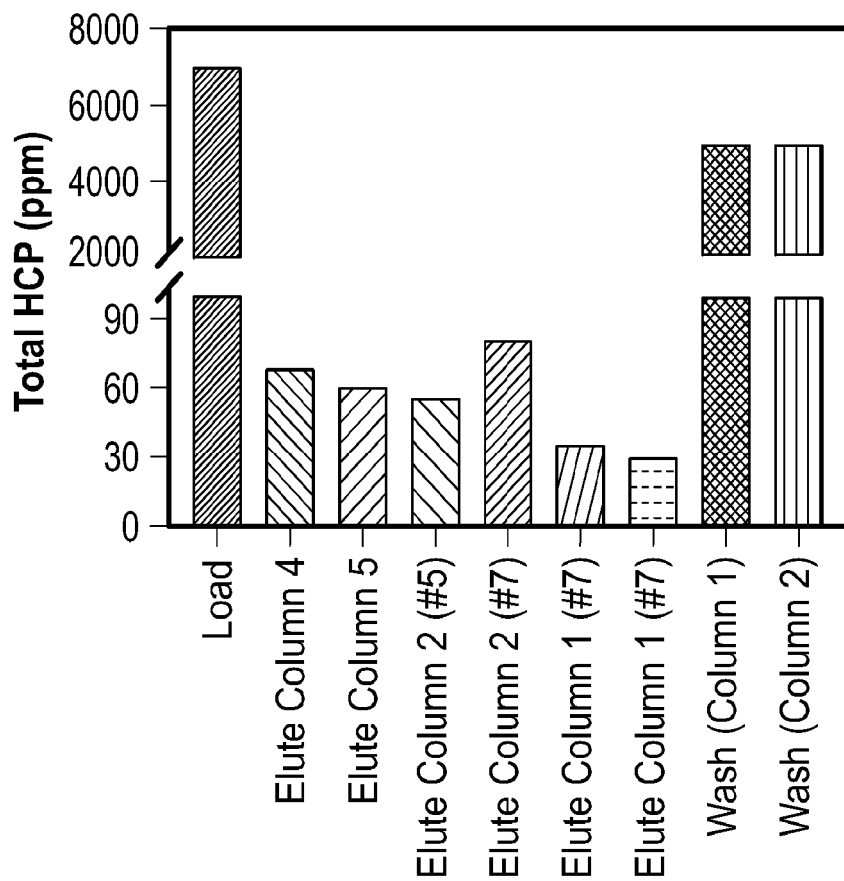
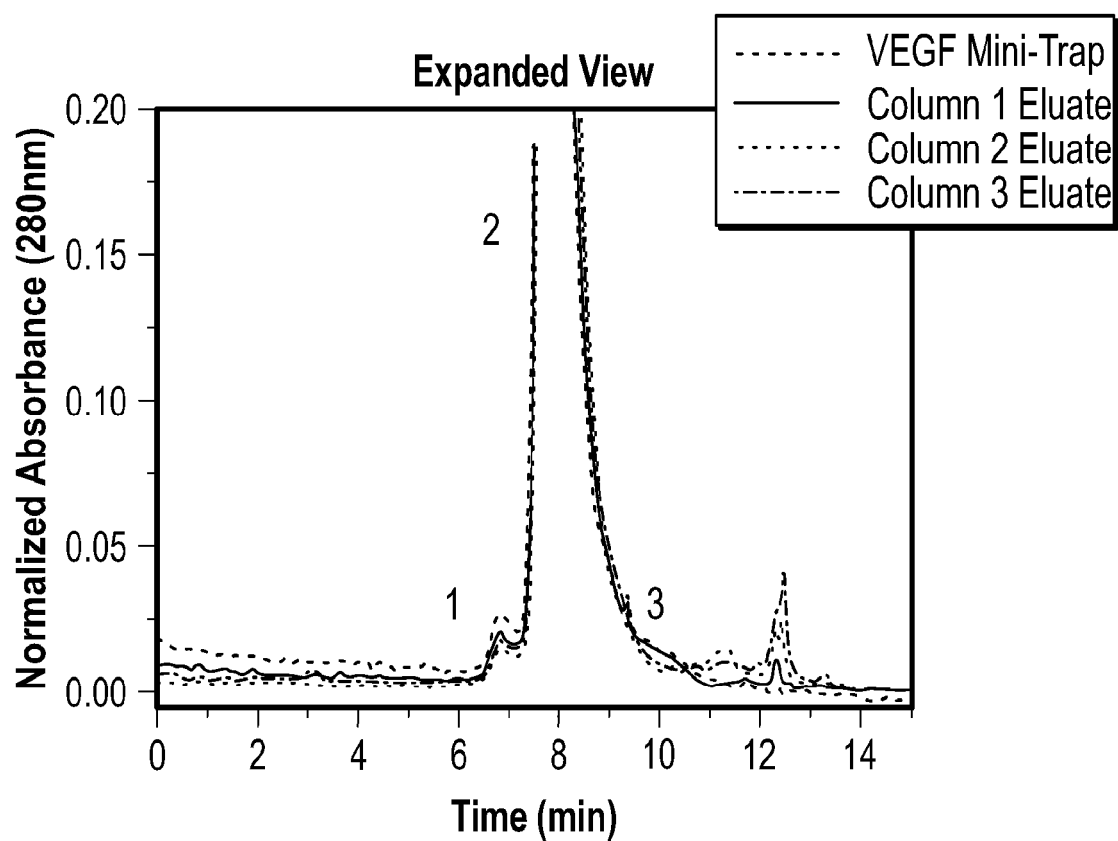
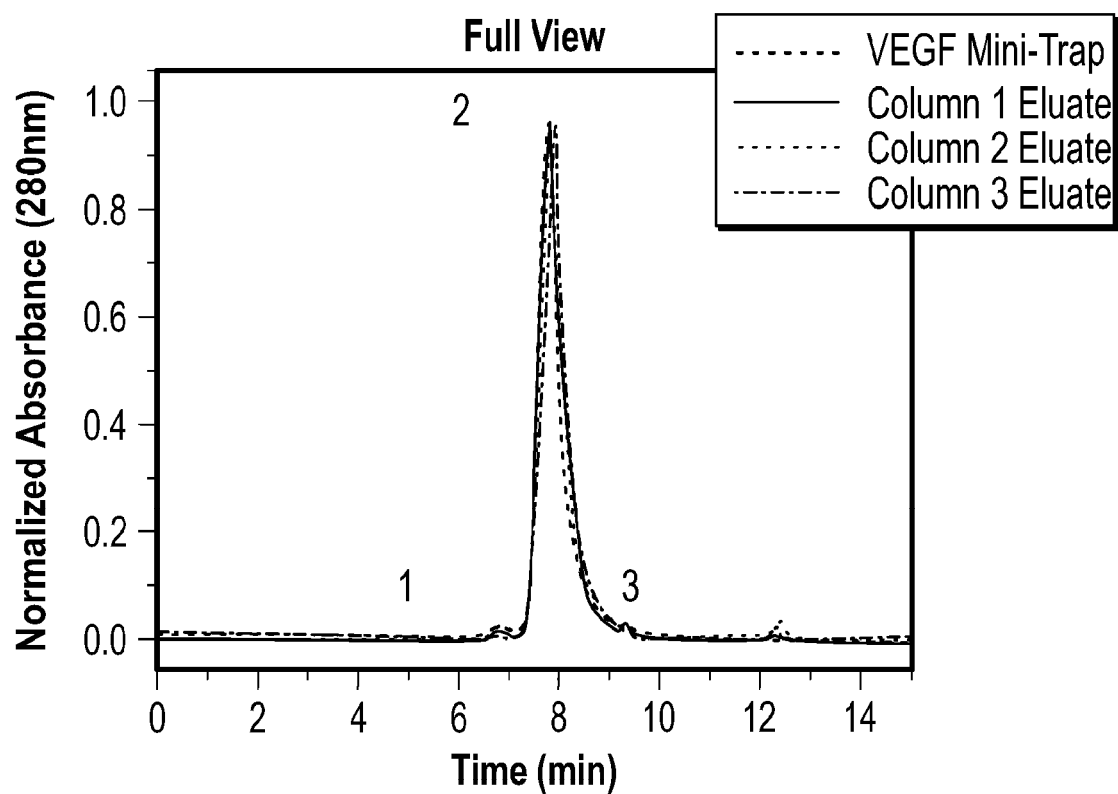


FIG. 35B



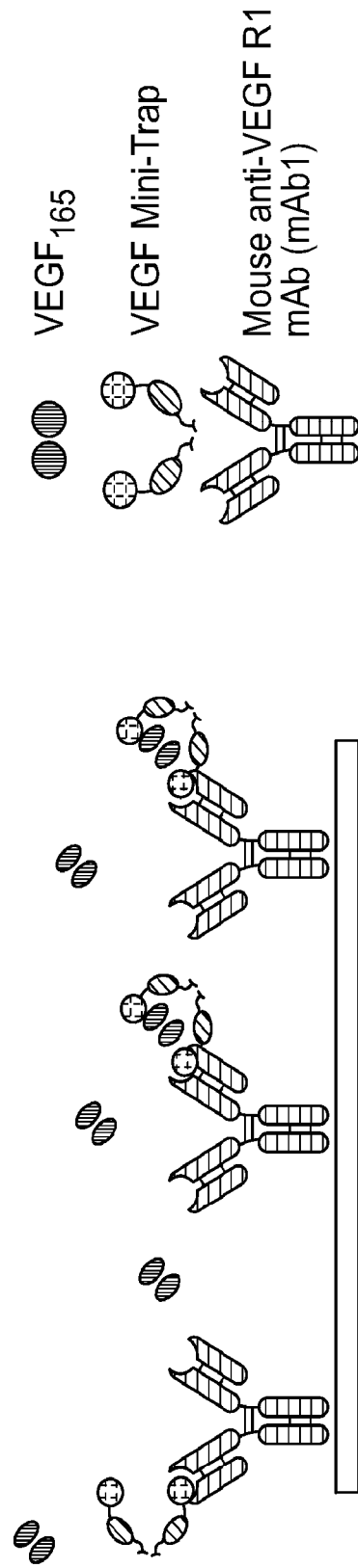
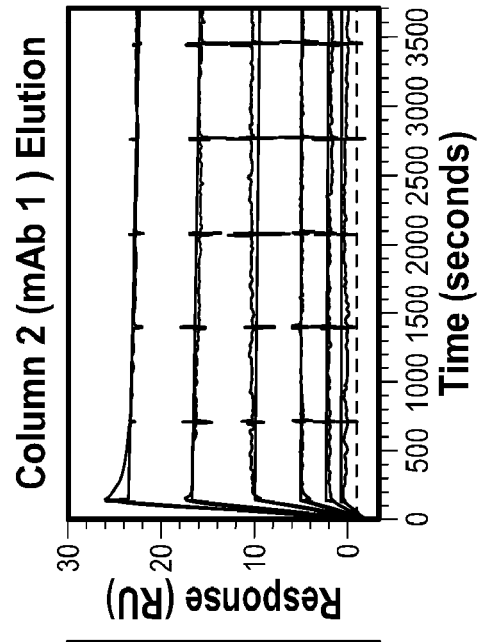
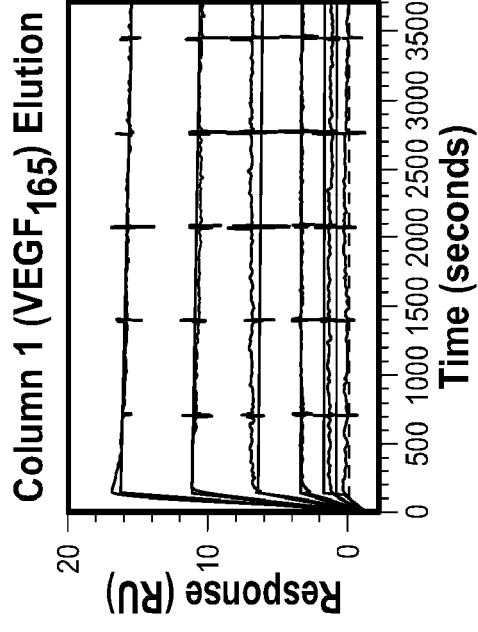
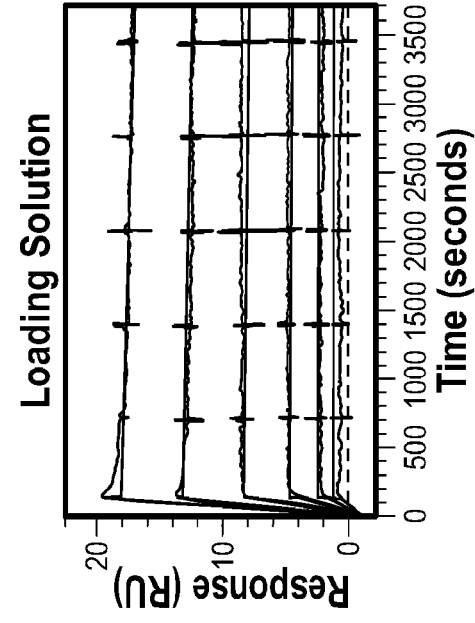


FIG. 37



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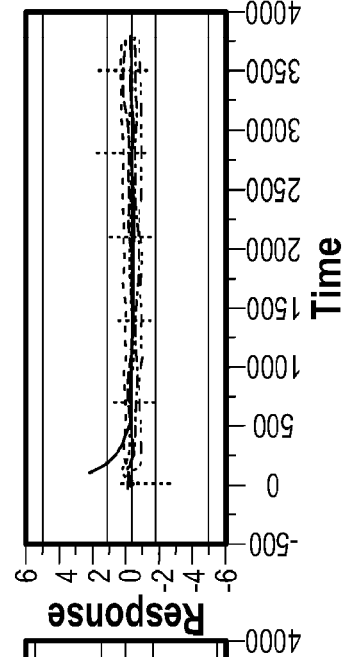
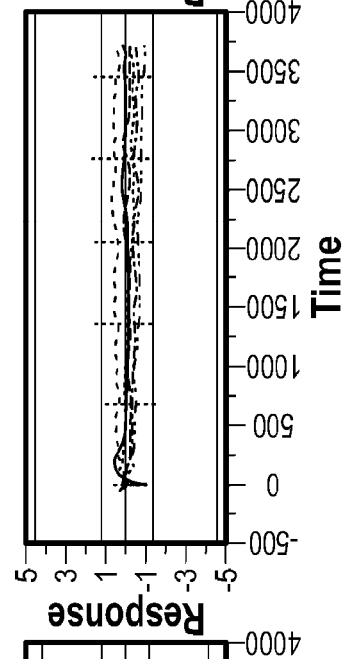
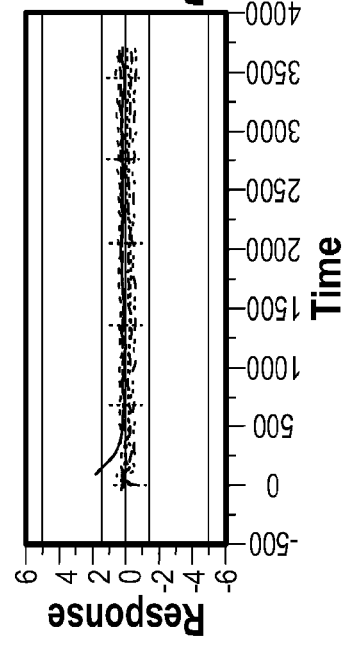


FIG. 38

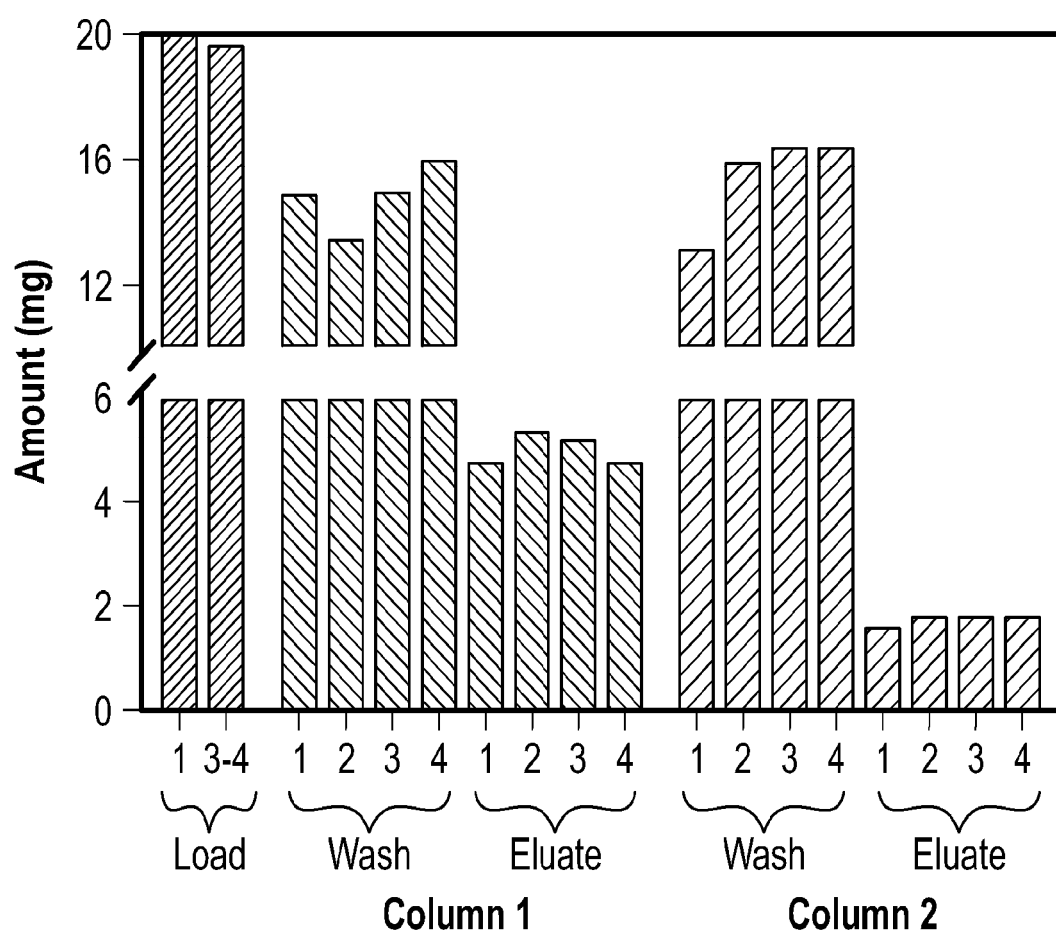


FIG. 39

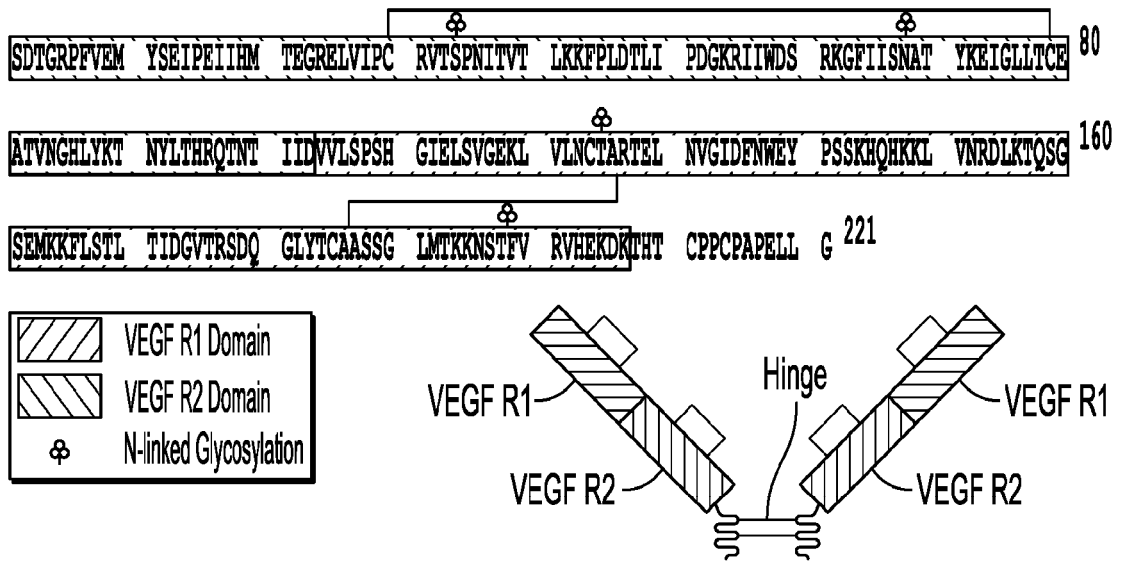


FIG. 40

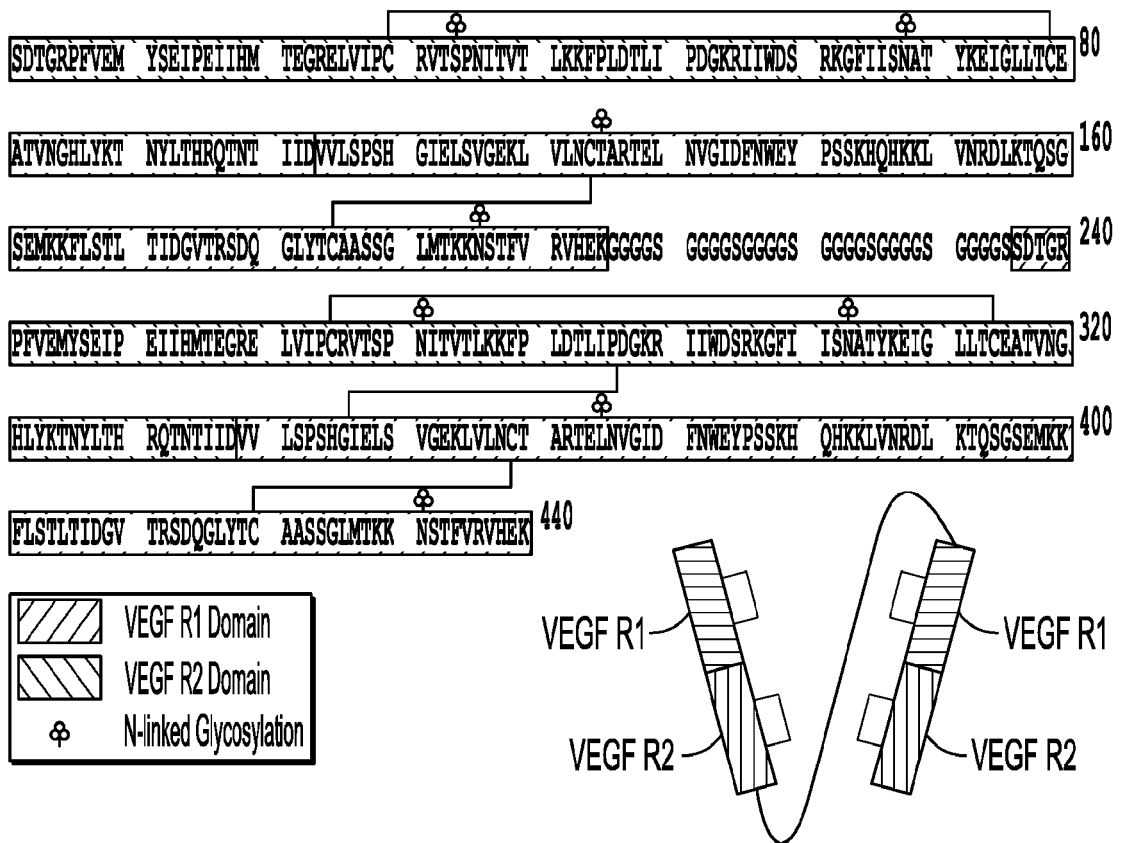
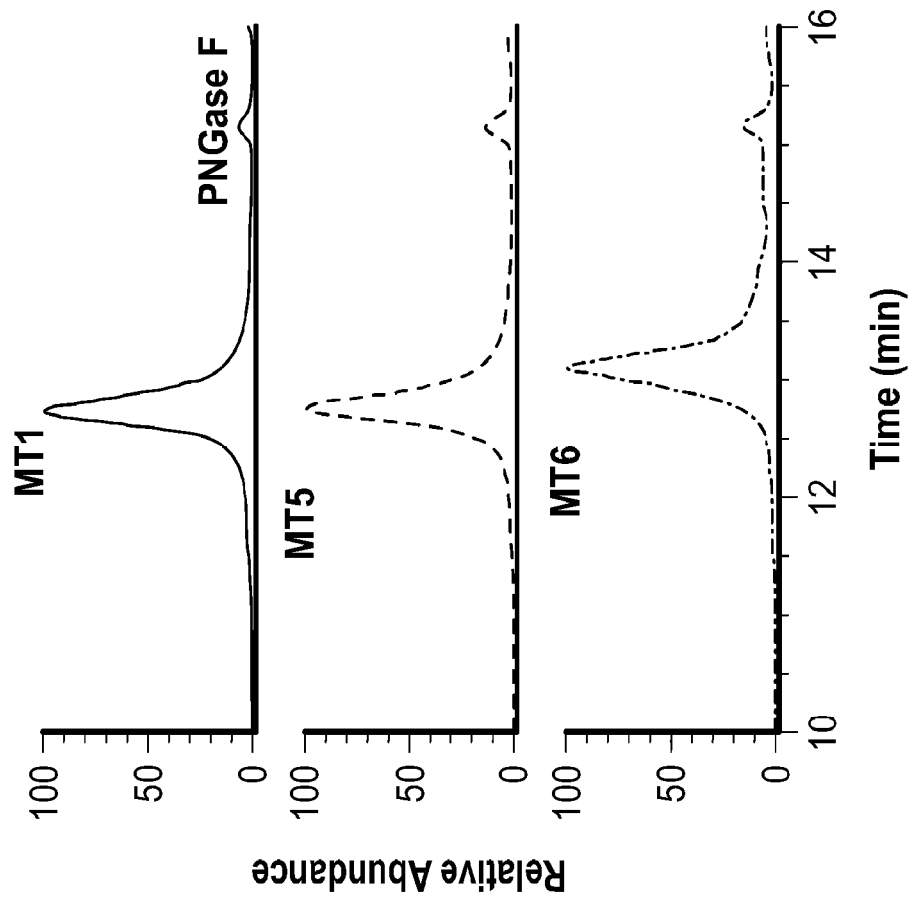


FIG. 41

TICs of Native SEC-MS Analysis



Zoom-in LMW Region:

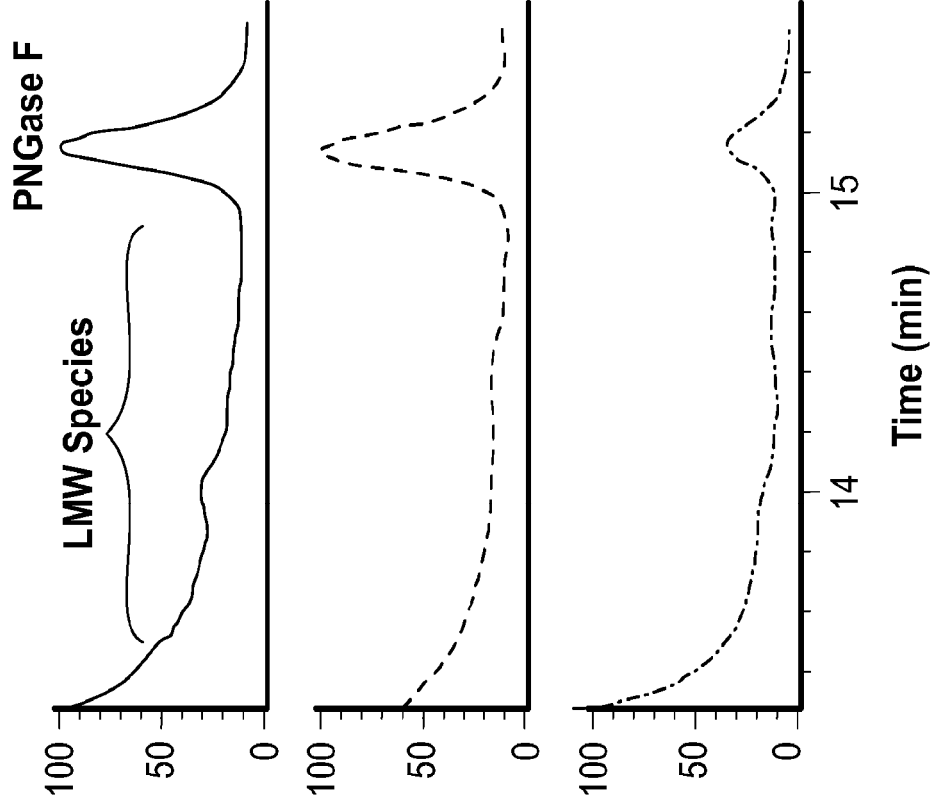


FIG. 42

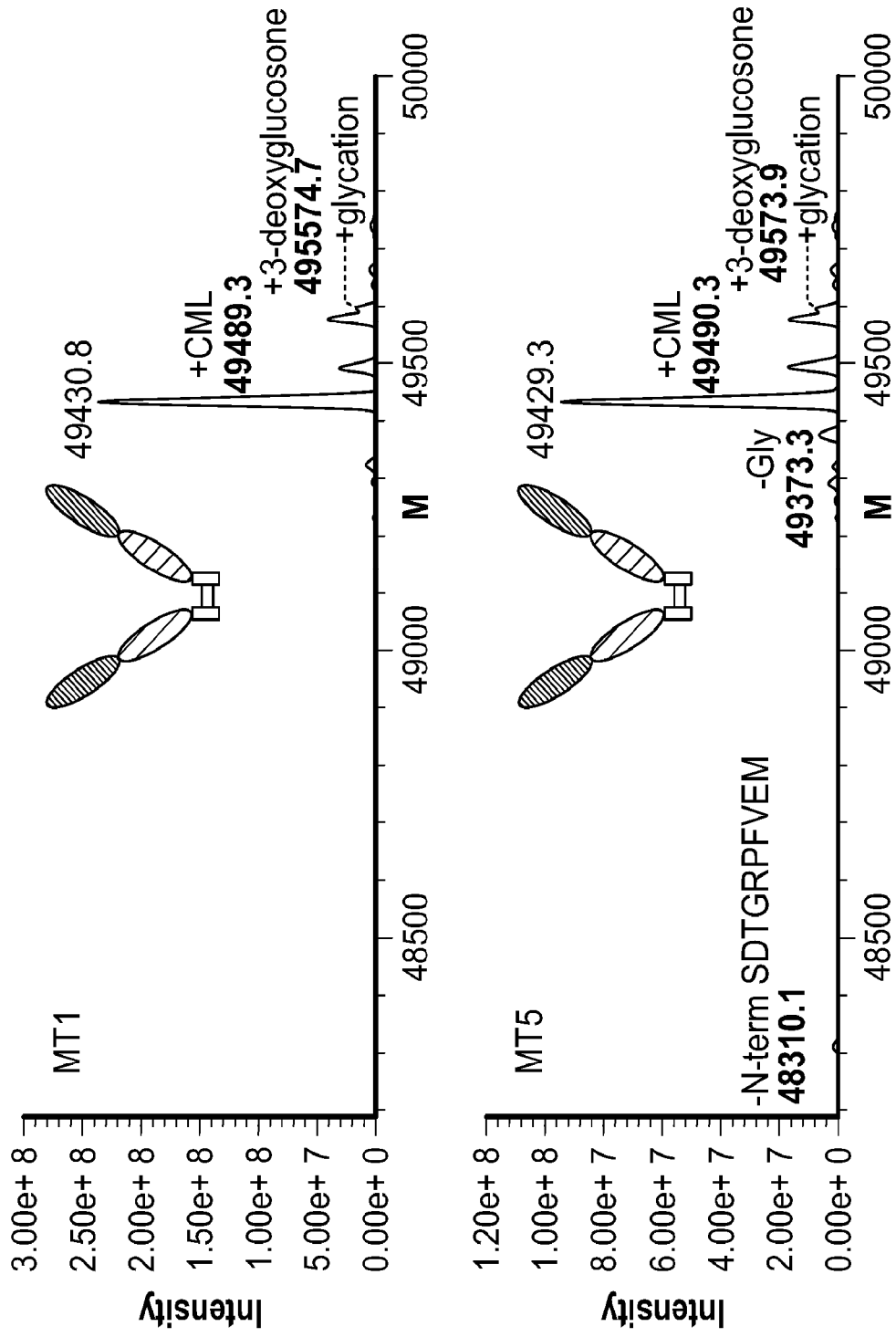


FIG. 43

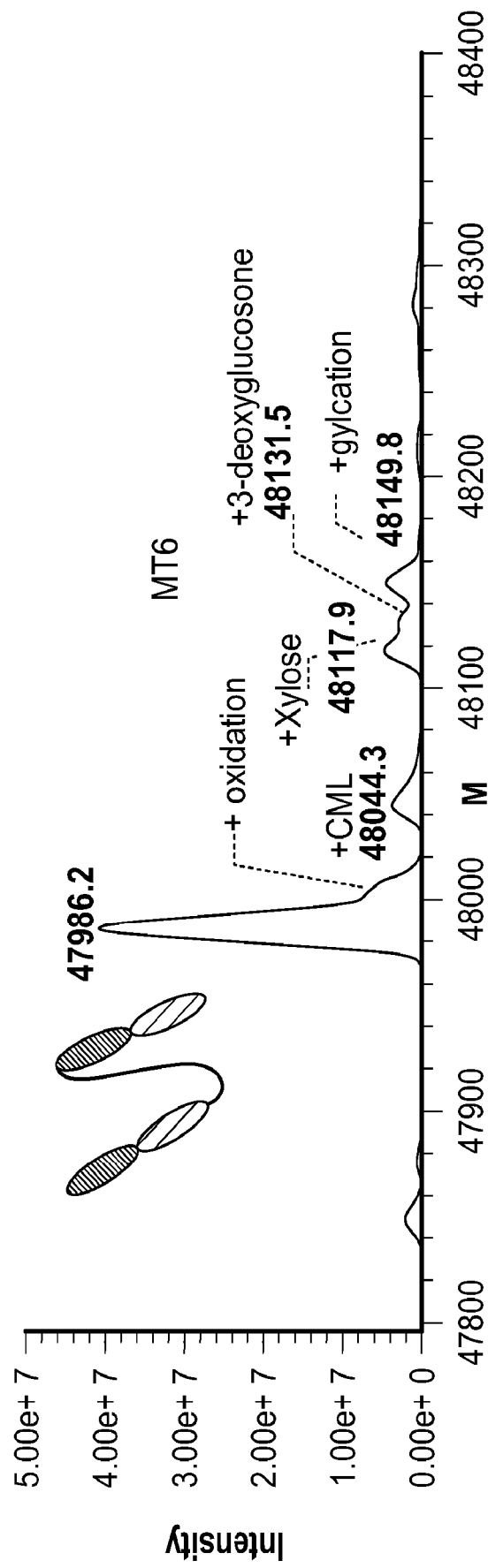


FIG. 44

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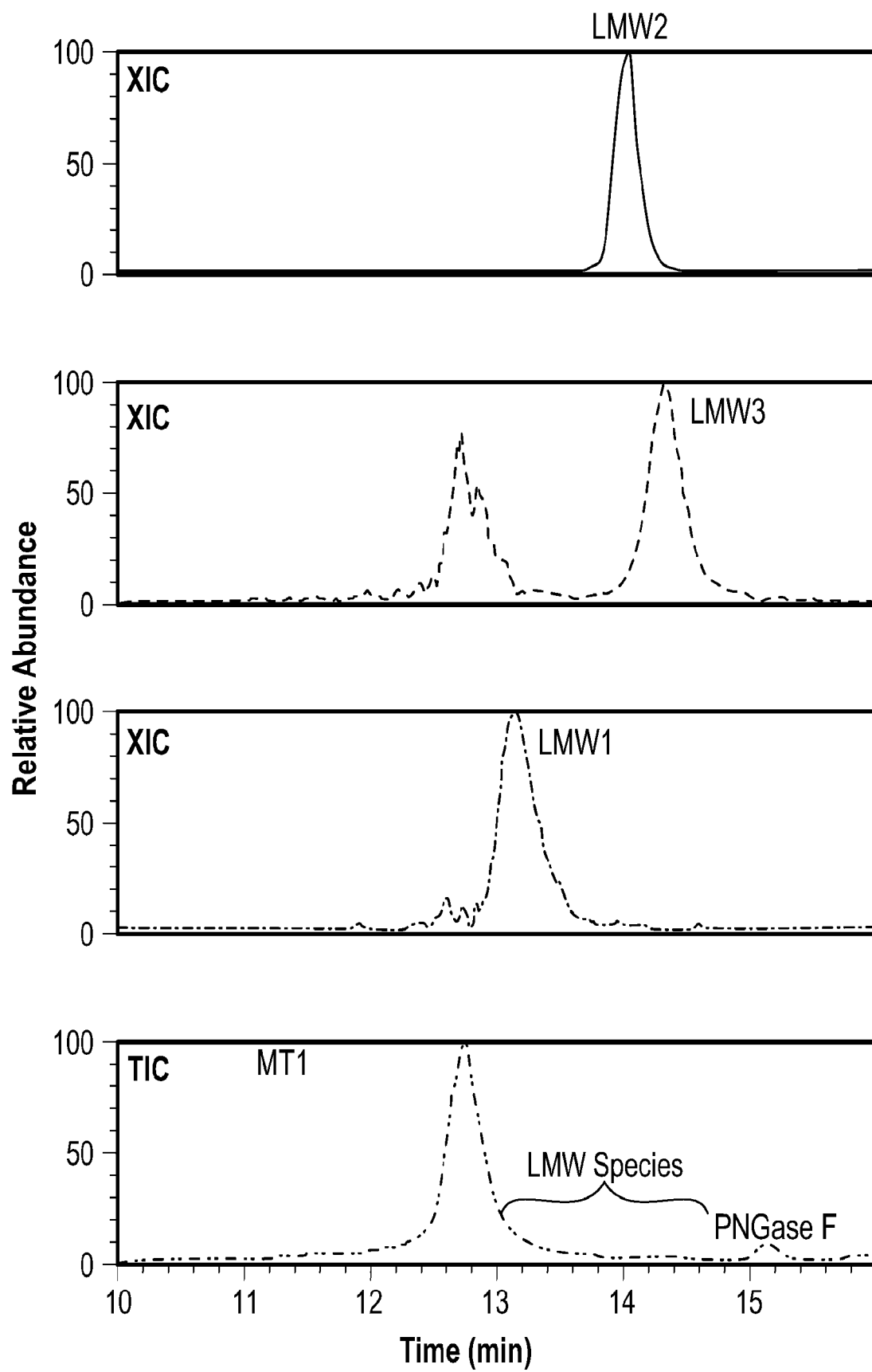


FIG. 45A

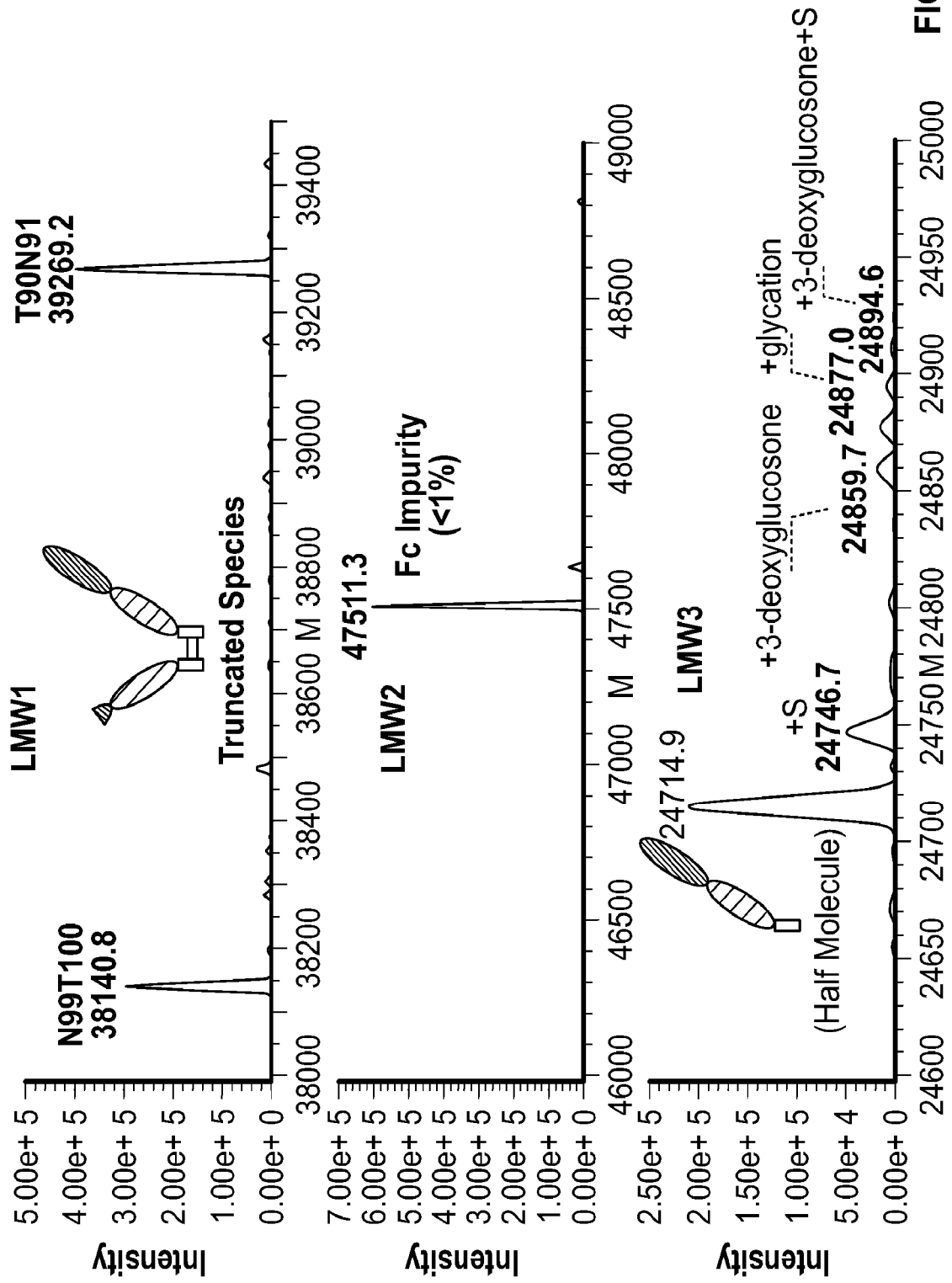


FIG. 45B

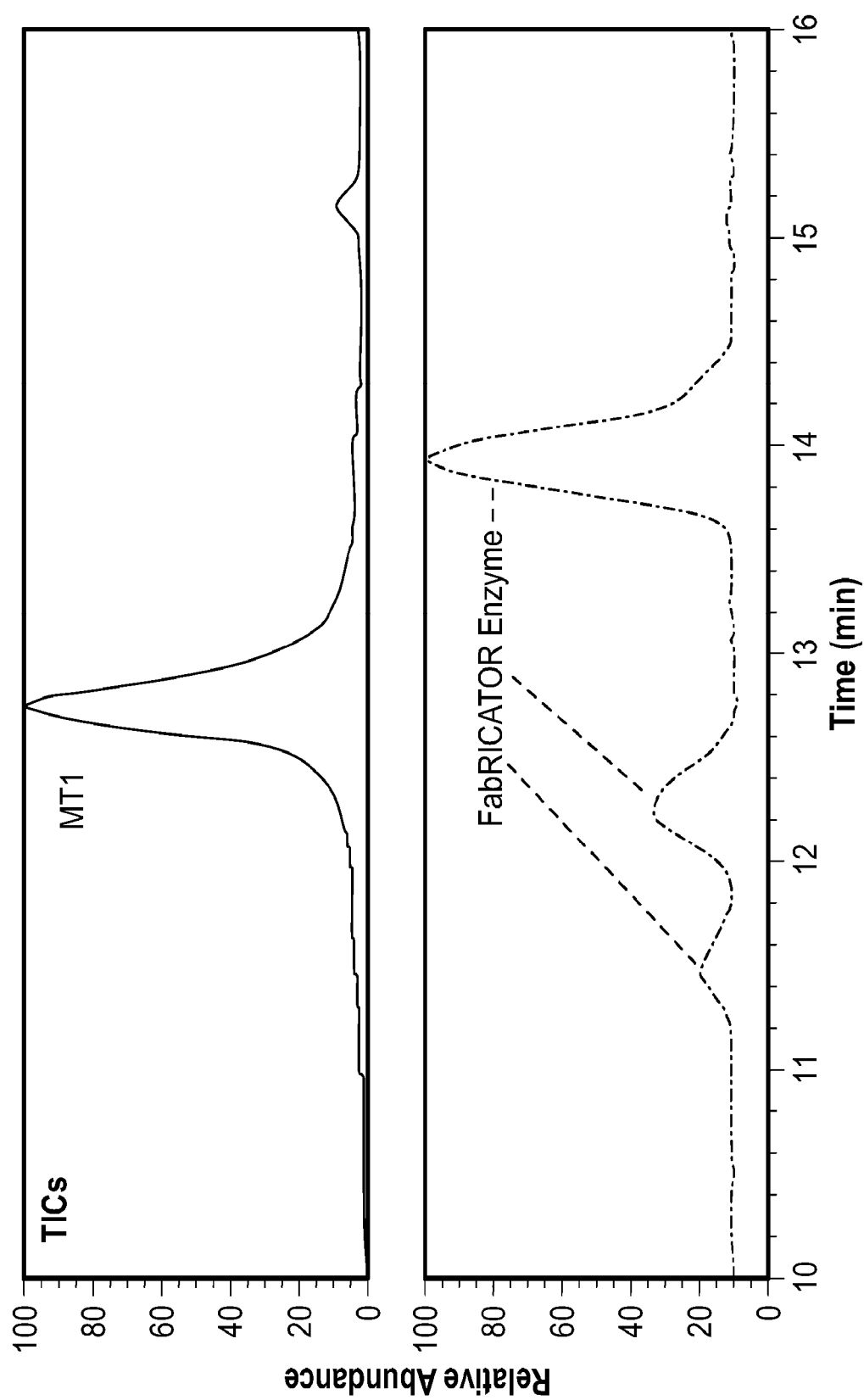


FIG. 46

45/60

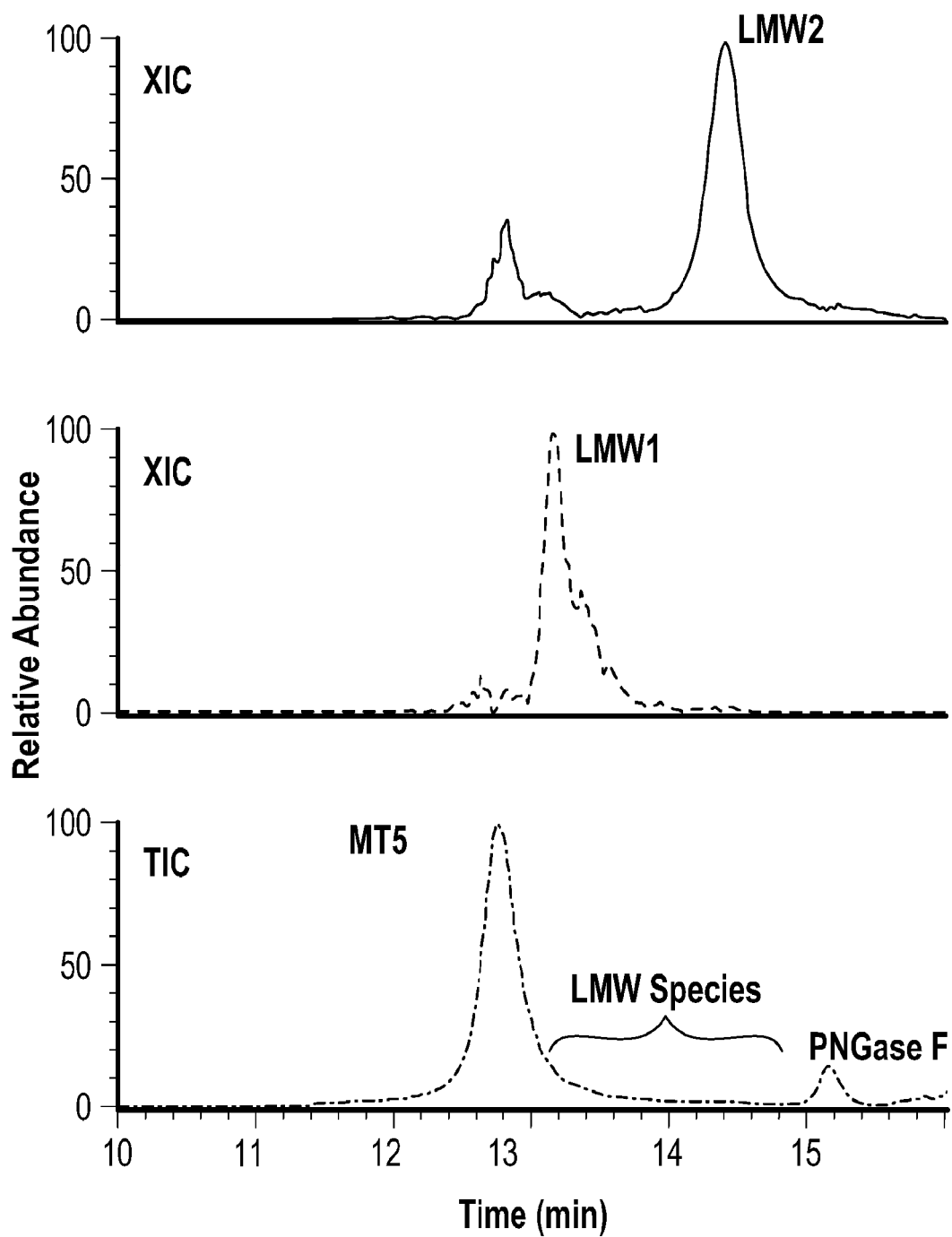


FIG. 47

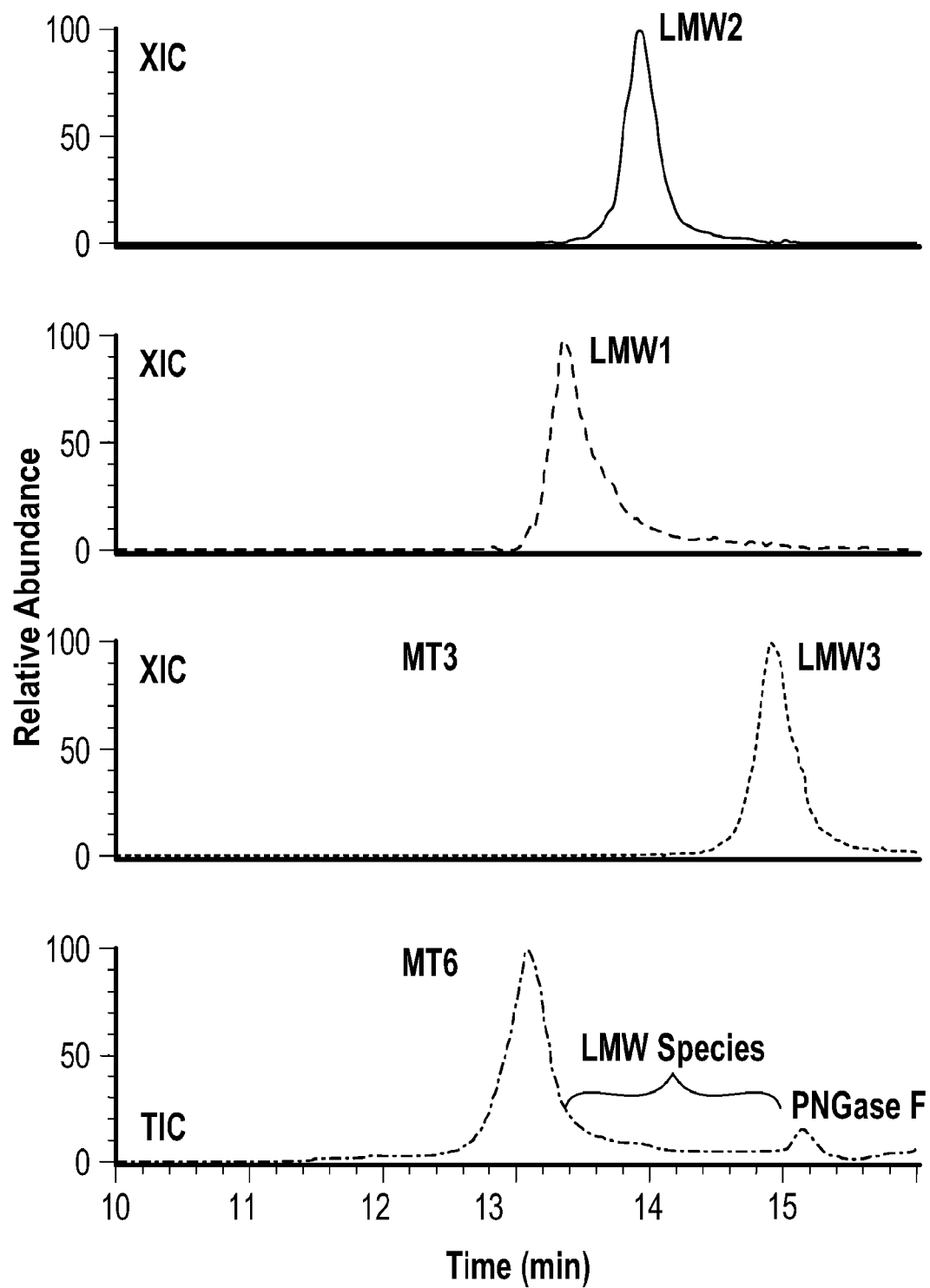
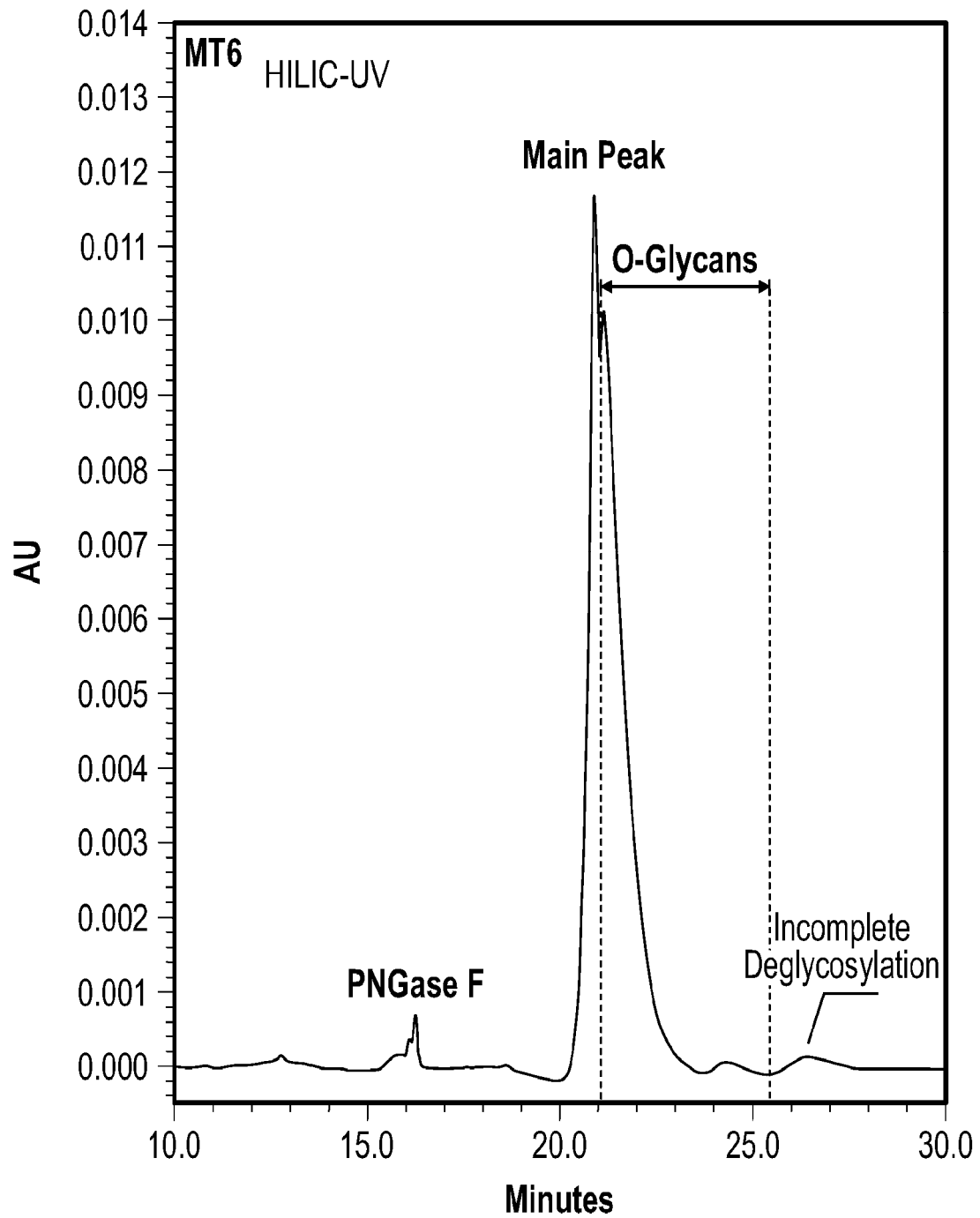
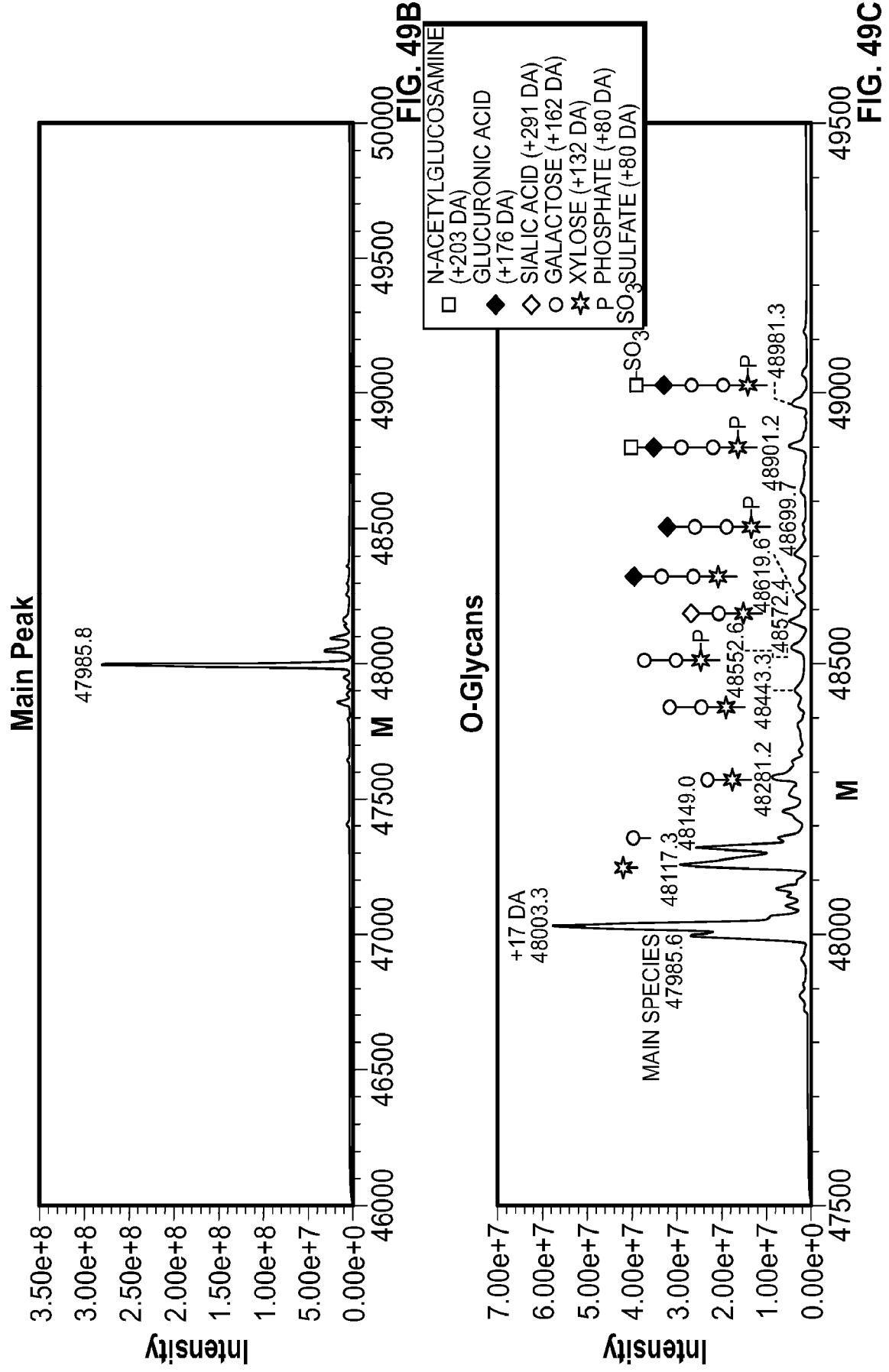


FIG. 48

**FIG. 49A**



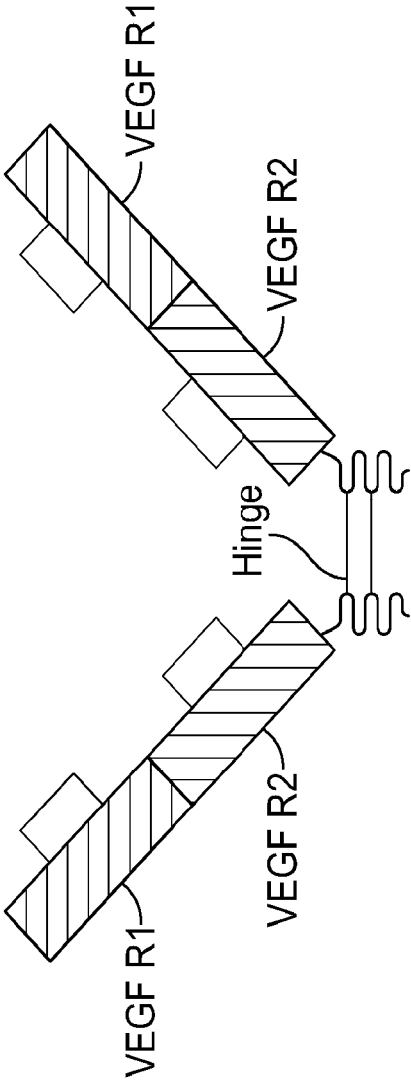
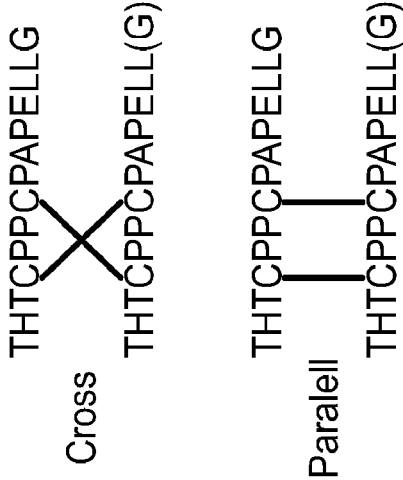
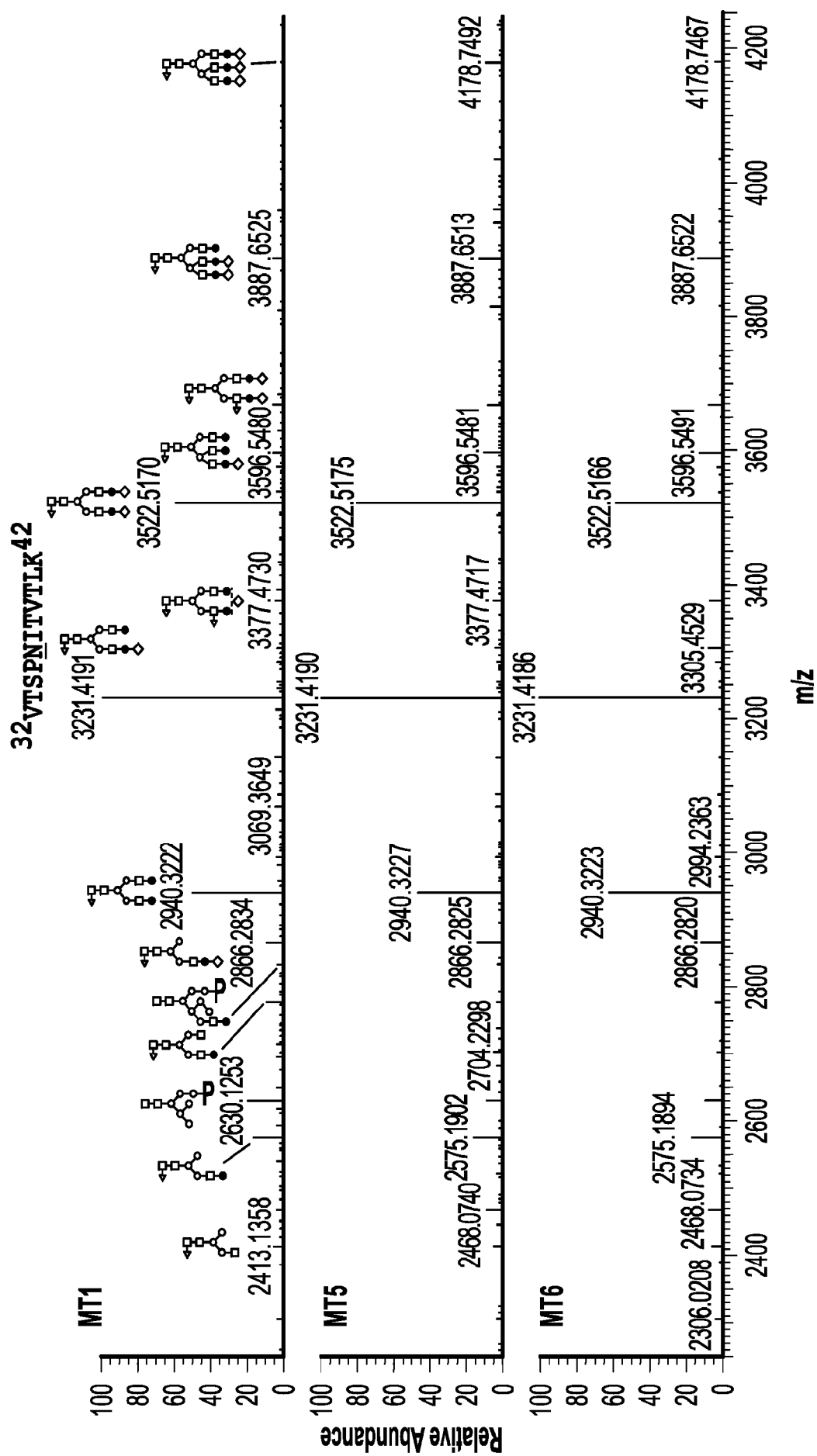


FIG. 50





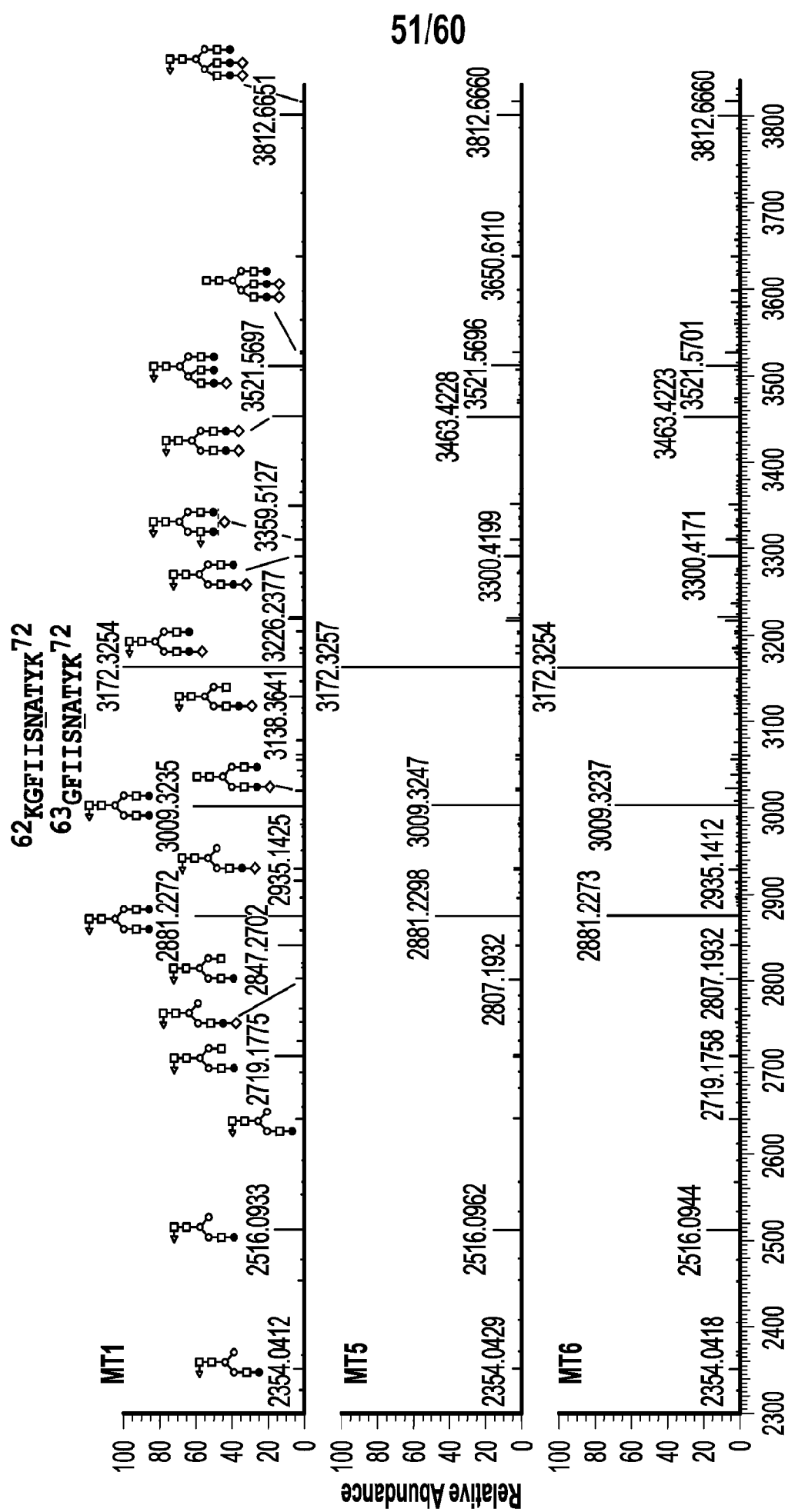


FIG. 52

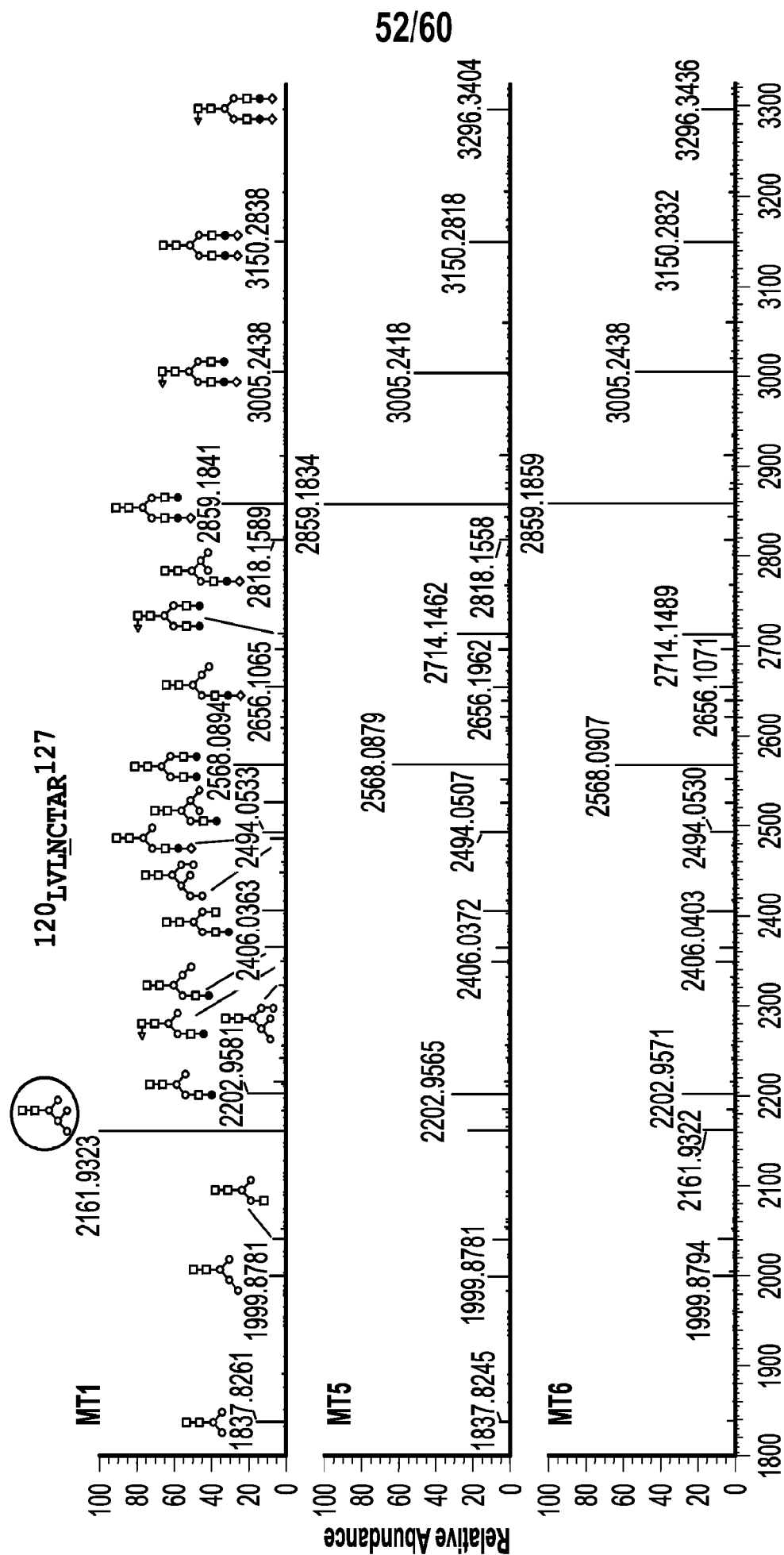


FIG. 53

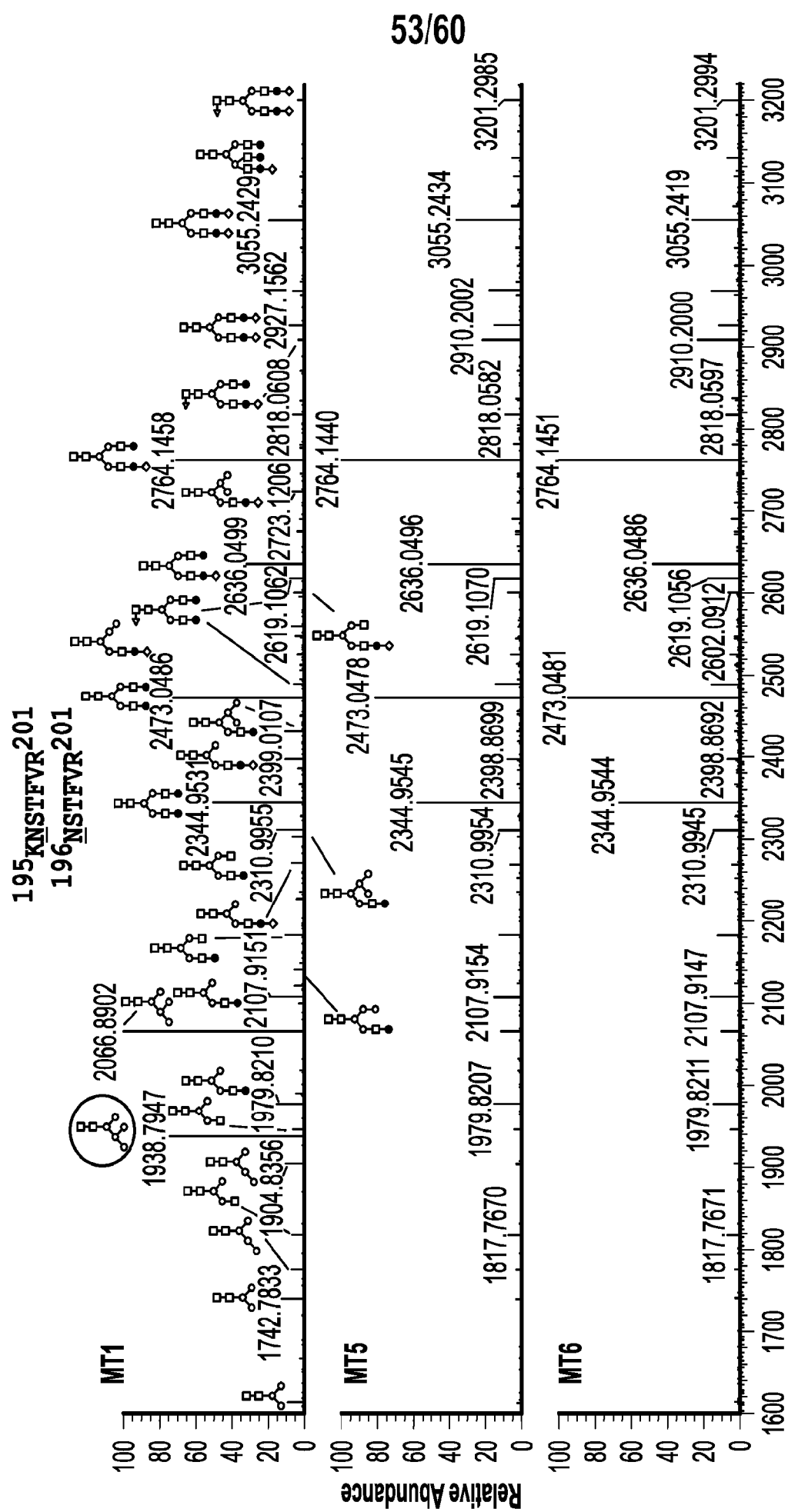


FIG. 54

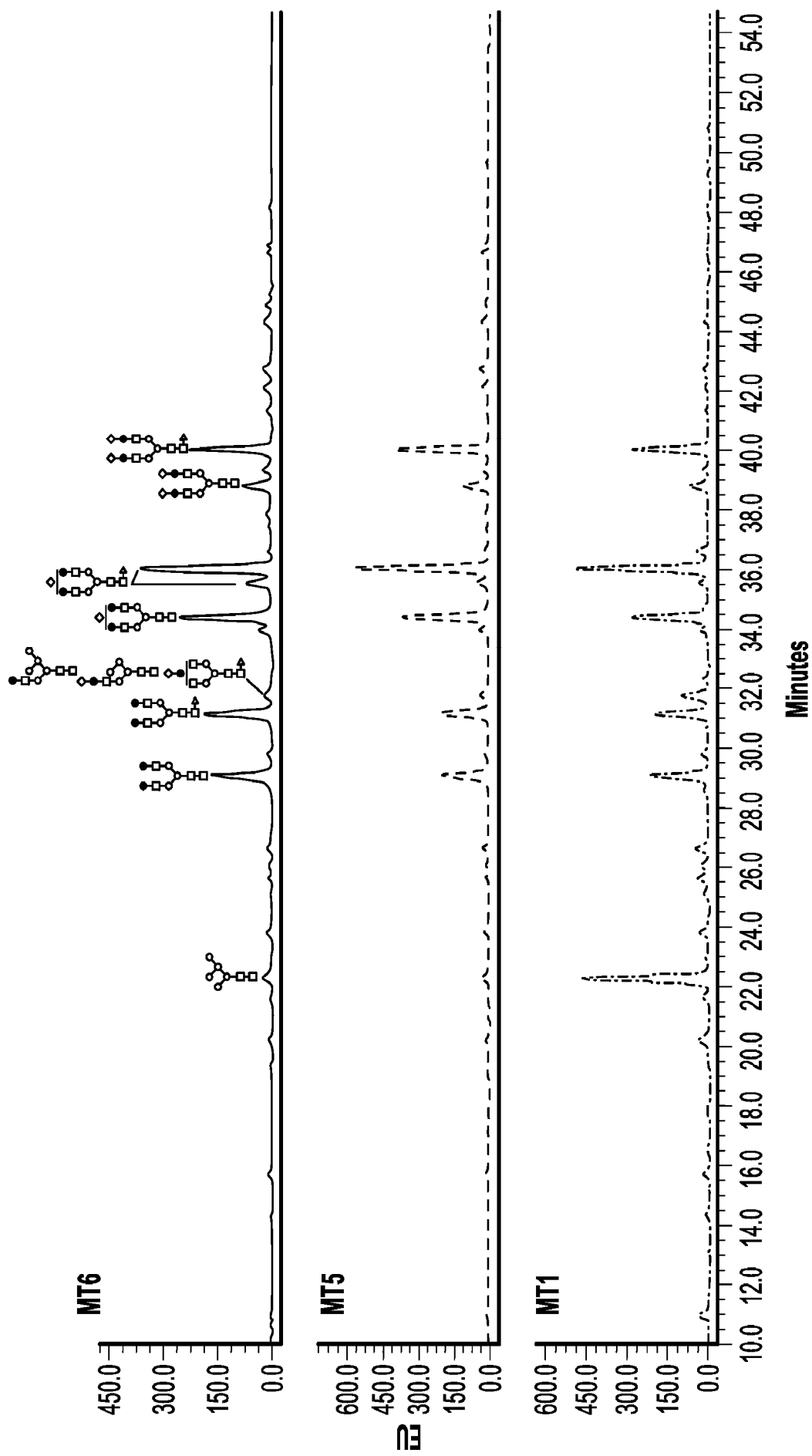


FIG. 55

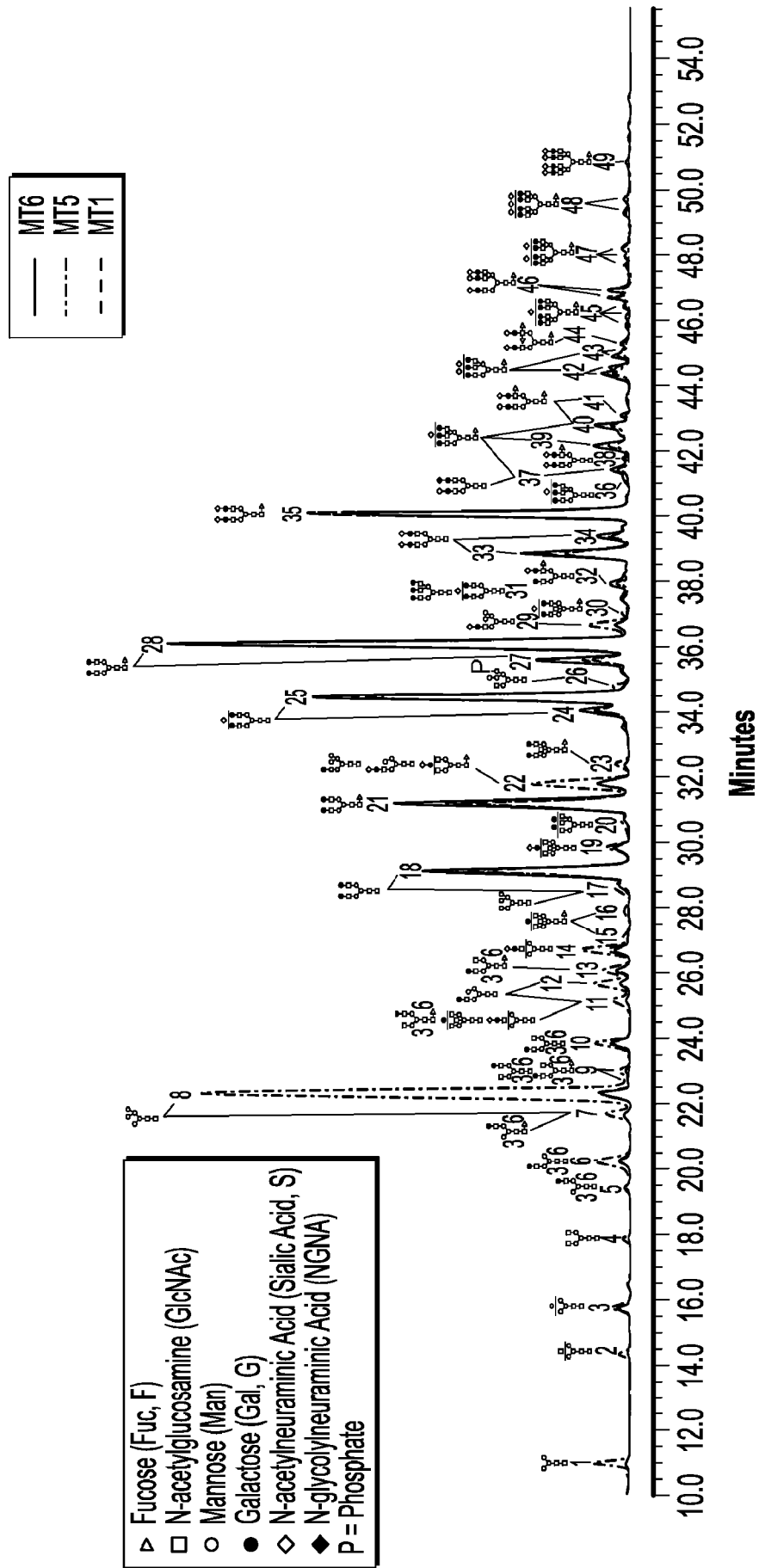


FIG. 56

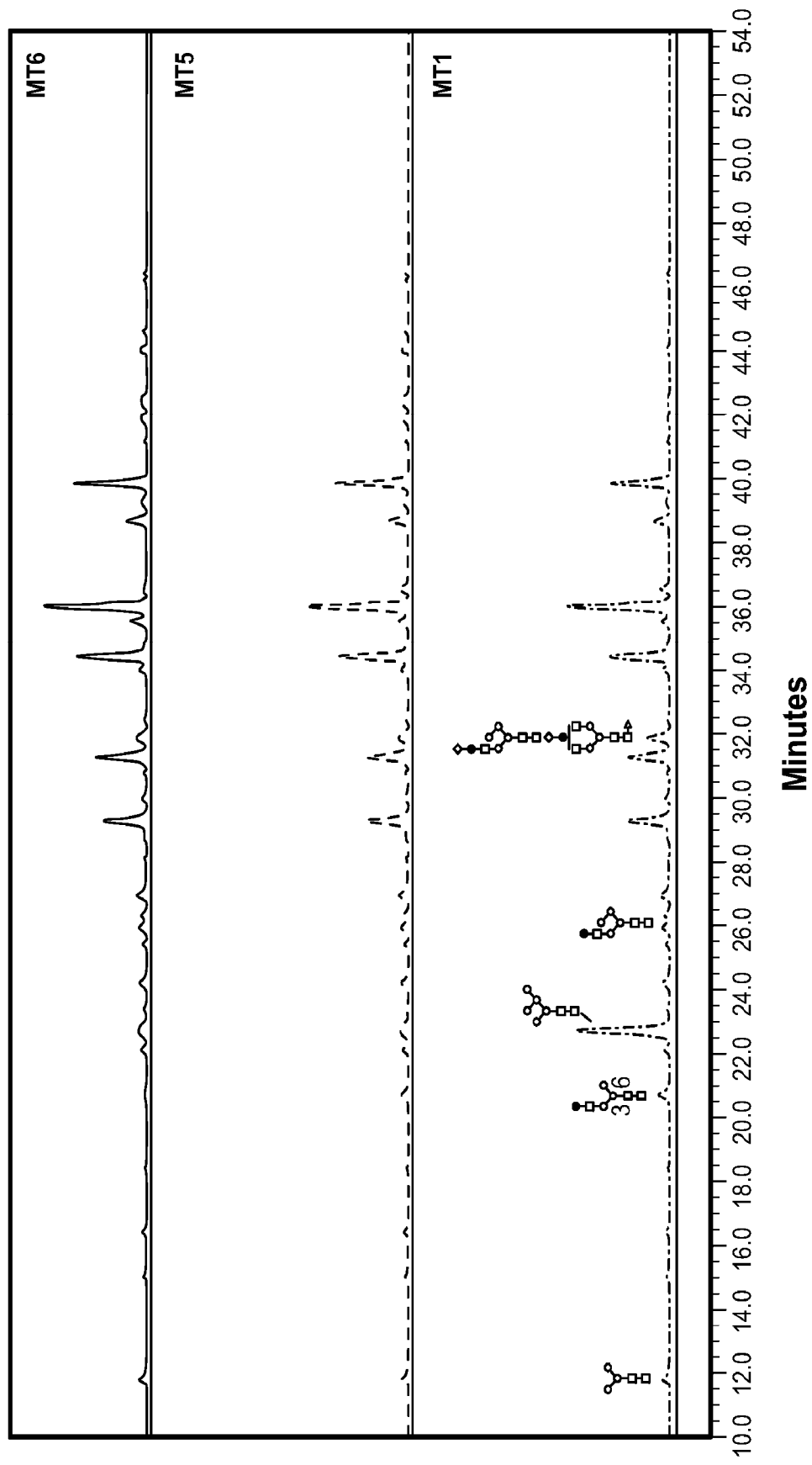


FIG. 57

Peak No.	Abbreviation	Glycan Structure	% Peak Area			Theoretical Mass (Da)
			MT6	MT5	MT1	
1	G0-2GlcNAc		0.11	0.19	0.96	1221.50
2	G0-GlcNAc		0.09	0.11	0.34	1424.58
3	Man4		0.51	0.56	0.62	1383.56
4	G0		0.07	0.05	0.26	1627.66
5	G1-GlcNAc (1-6)		0.26	0.31	0.14	1586.63
6	G1-GlcNAc (1-3)		0.55	0.61	1.76	1586.63
7	G1F-GlcNAc (1-6)		0.34	0.37	0.92	1732.69
8	Man5		1.32	1.63	16.11	1545.61
9	G1F-GlcNAc (1-3)		0.35	0.26	0.45	1732.69
	G1 (1-6)					1789.71
10	G1 (1-3)		0.89	0.88	1.34	1789.71
11	bG1		0.26	0.22	0.78	1992.79
	G1S1-GlcNAc					1877.73
	G1F (1-6)					1935.77
	Man4_G1		0.51	0.46	1.53	1748.69
12						
13	G1F (1-3)		0.67	0.64	1.11	1935.77
14	G1S1-GlcNAc		0.73	1.20	1.86	1877.73
15	bG1F		0.00	0.00	0.32	2138.85

FIG. 58A

Peak No.	Abbreviation	Glycan Structure	% Peak Area			Theoretical Mass (Da)
			MT6	MT5	MT1	
16	bG1F		0.00	0.00	0.40	2138.85
17	Man6		0.51	0.41	0.85	1707.66
	G2					1951.77
18			9.95	8.85	7.96	
19	G1S1-GlcNAc		0.84	0.89	1.04	2080.81
20	G2+GlcNAc		0.28	0.28	0.57	2154.85
21	G2F		11.24	9.13	7.47	2097.82
22	Man5_G1		1.61	1.82	4.13	1910.74
	Man4_G1S1					2039.78
	G1FS1					2226.87
23	bG2F		0.27	0.32	0.66	2300.90
24	G2S1+Fuc		2.63	2.13	1.75	2242.86
25			13.42	14.46	9.50	
26	Man6_G0+Phos		0.00	0.00	0.53	1787.63
27	G2FS1		4.00	2.43	1.67	2388.92
28			18.85	21.19	15.94	2388.92
29	Man5_G1S1		0.51	0.62	1.70	2201.84
30	bG2FS1		0.00	0.00	0.27	2592.00
31	G2+NGNA		0.44	0.35	0.35	2258.86
	G3					2316.90

FIG. 58B

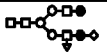
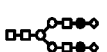
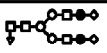
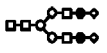
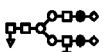
Peak No.	Abbreviation	Glycan Structure	% Peak Area			Theoretical Mass (Da)
			MT6	MT5	MT1	
32	G2S1+Fuc		0.85	0.59	0.38	2388.92
33	G2S2		4.56	4.36	2.57	2533.96
34			1.31	0.99	0.71	2533.96
35	G2FS2		10.76	13.67	8.33	2680.02
36	G3S1		0.20	0.14	0.11	2607.99
37	G2S1+NGNA		0.87	0.59	0.35	2549.95
	G3FS1					2754.05
38	G2S2+Fuc		0.23	0.13	0.07	2680.02
39	G3FS1		1.61	1.22	0.67	2754.05
40			1.77	1.77	0.95	2754.05
41	G2FS2+Fuc		0.24	0.24	0.15	2826.07
42	G3FS2		1.85	1.59	0.77	3045.15
43			0.78	0.77	0.32	
44	G2FS2+2Fuc		0.34	0.31	0.14	2972.13
45	G4FS1		0.57	0.29	0.12	3119.18
46	G3FS3		1.14	1.43	0.58	3336.24
47	G4FS2		0.89	0.72	0.24	3410.28
48	G4FS3		0.63	0.60	0.18	3701.38
49	G4FS4		0.22	0.23	0.07	3992.47

FIG. 58C

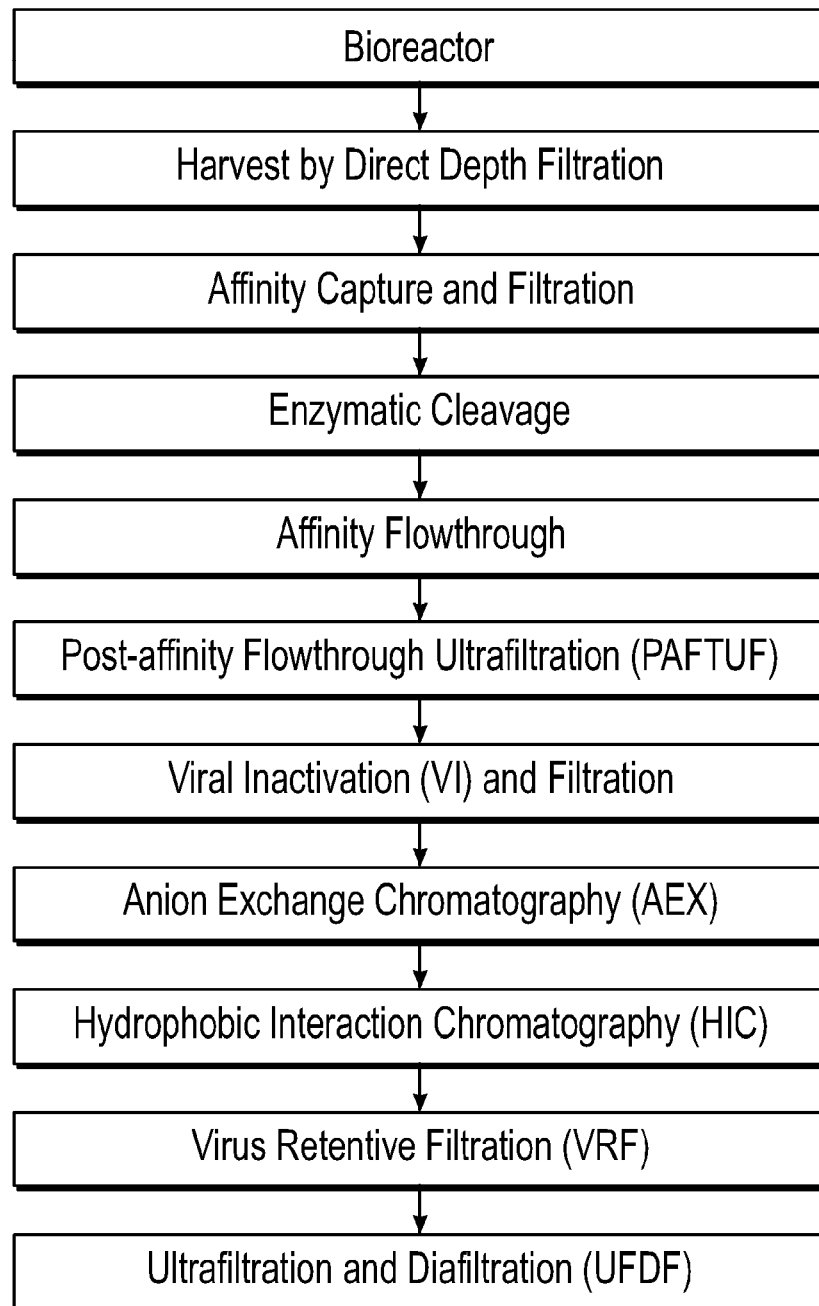


FIG. 59