UNIVERSITÉ DE GENÈVE

LSMS

CAN WE PREDICT THE PREFERENCE FOR ADDUCT FORMATION IN ELECTROSPRAY?

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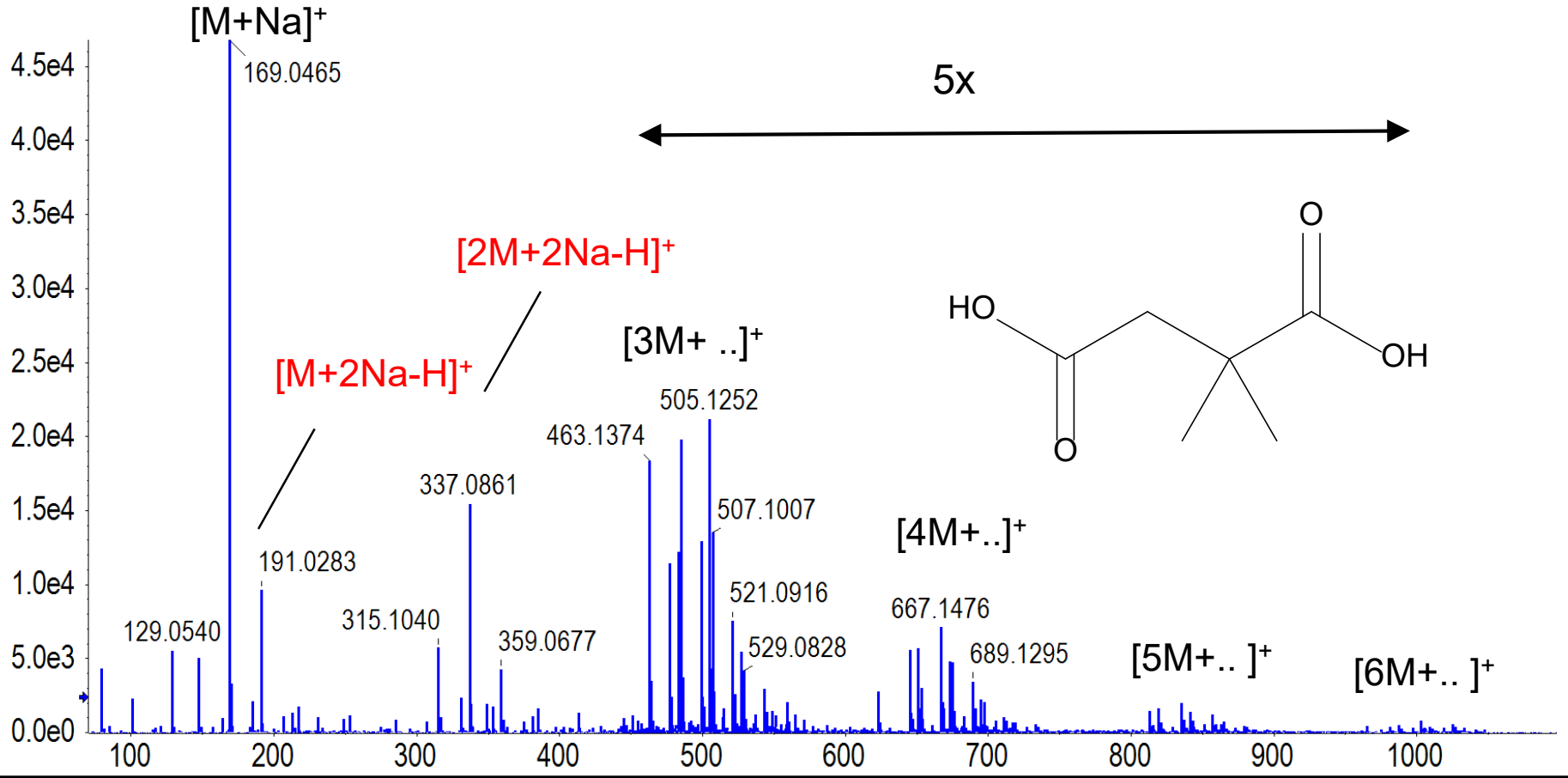
Outline :

1) Short Introduction

2) ESI spectra of succinic acid with and without additives

3) Model selection and theoretical results

Electrospray Flow Injection Analysis of 2,2-Dimethylsuccinic Acid



ADDUCTS

$HCOO^-$ and AcO^- adducts originate from LC mobile phase modifiers while Cl^- adducts can form due to extraction solvents; additionally, residues of salts from sample preparation may lead to salt (sodium, potassium) adducts

Adduct formation was further found to be dependent on the sum of surfaces of polar atoms in a molecule MW and O/N composition

ELSEVIER

Journal of Chromatography A

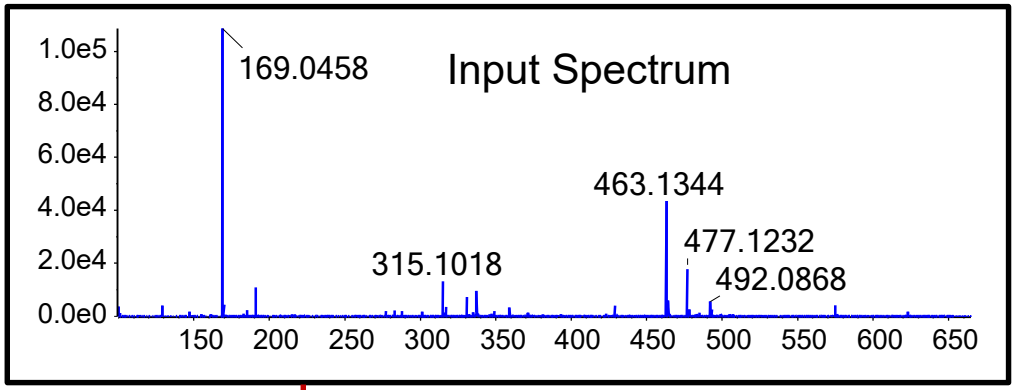
Volume 1600, 30 August 2019, Pages 174-182

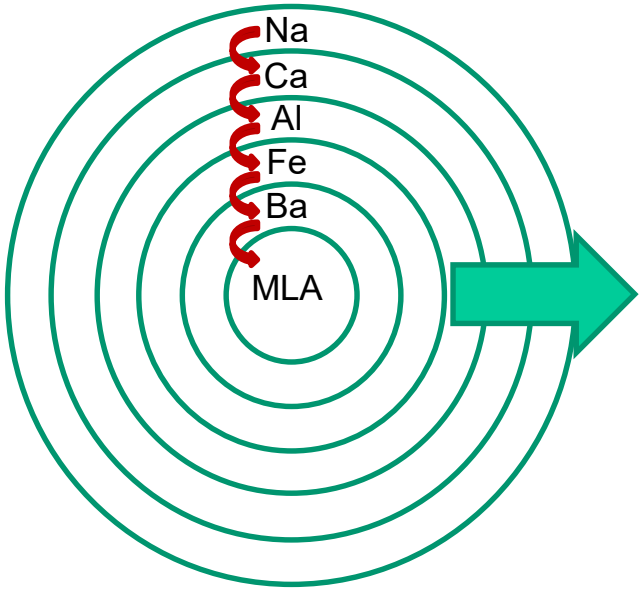
Adduct formation in electrospray ionisation-mass spectrometry with hydrophilic interaction liquid chromatography is strongly affected by the inorganic ion concentration of the samples

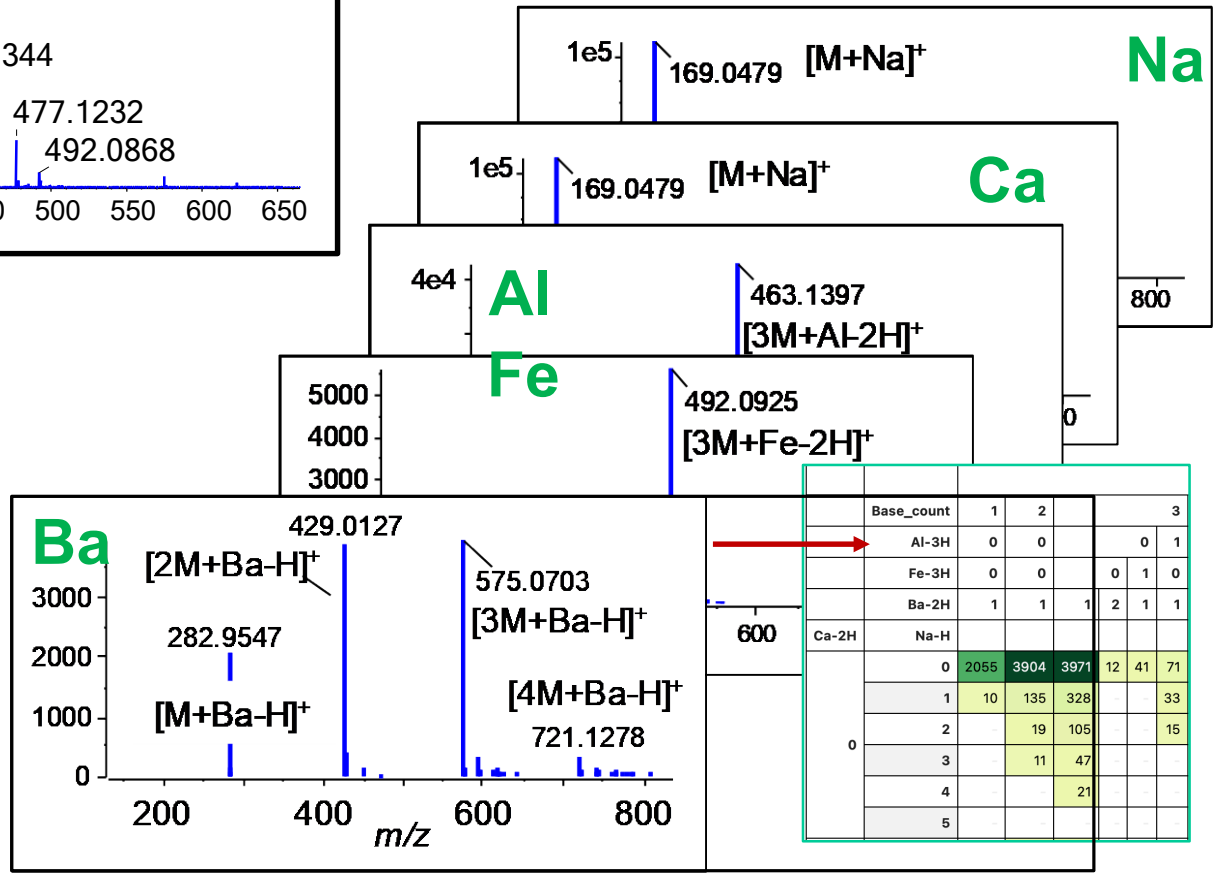
Ida Erngren [a], Jakob Haglöf [a], Mikael K.R. Engskog [a], Marika Nestor [b], Mikael Hedeland [a, c], Torbjörn Arvidsson [a, d], Curt Pettersson [a]

Multilayered Analysis

matches spectra to calculated target ion lists







	Base_count	1	2				3
	Al-3H	0	0			0	1
	Fe-3H	0	0		0	1	0
	Ba-2H	1	1	1	2	1	1
Ca-2H	Na-H						
0	0	2055	3904	3971	12	41	71
	1	10	135	328			33
	2		19	105			15
	3		11	47			
	4			21			
	5						

ELECTROSPRAY WINGS FOR MOLECULAR ELEPHANTS
from Ions in Solution to Gas Phase Ions

Analyte in Solution

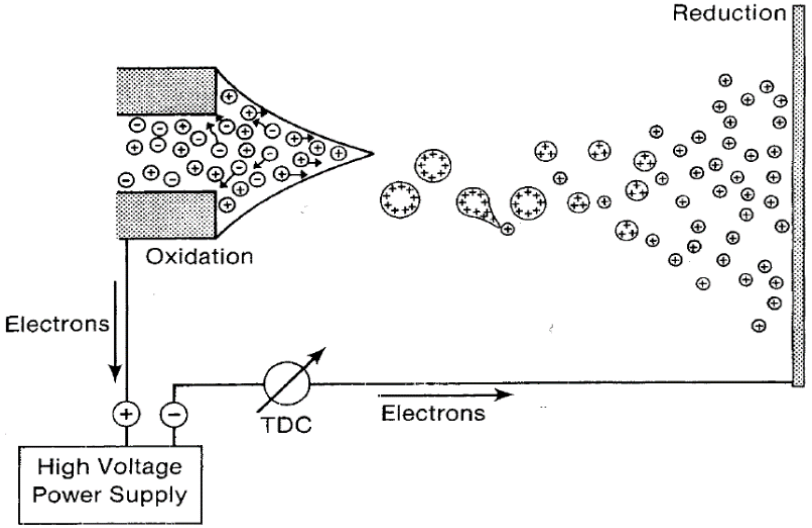
Solution Sprayed in ESI Source

Droplets Shrinkage

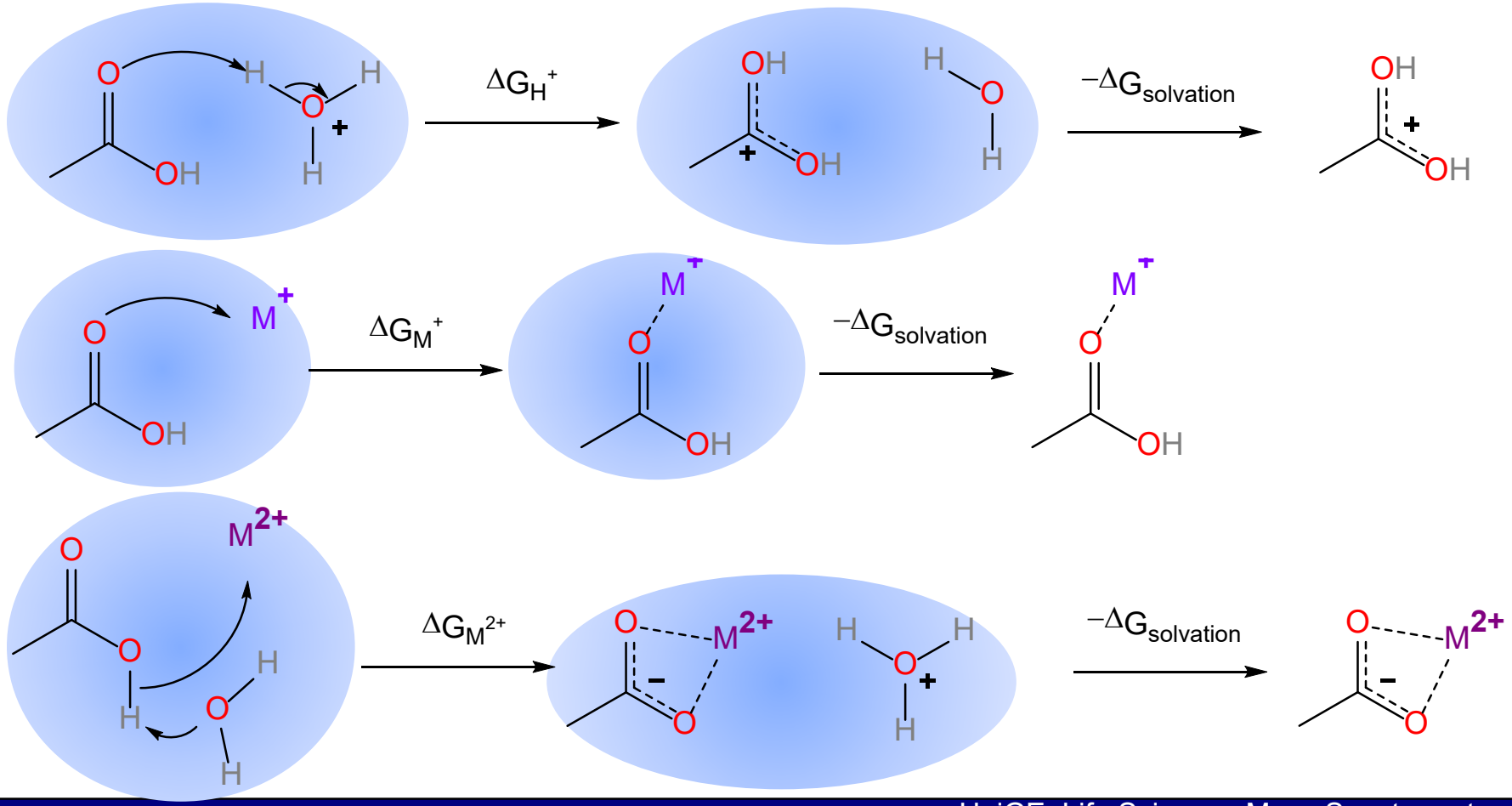
Ions from Droplets

Ions Desolvatation

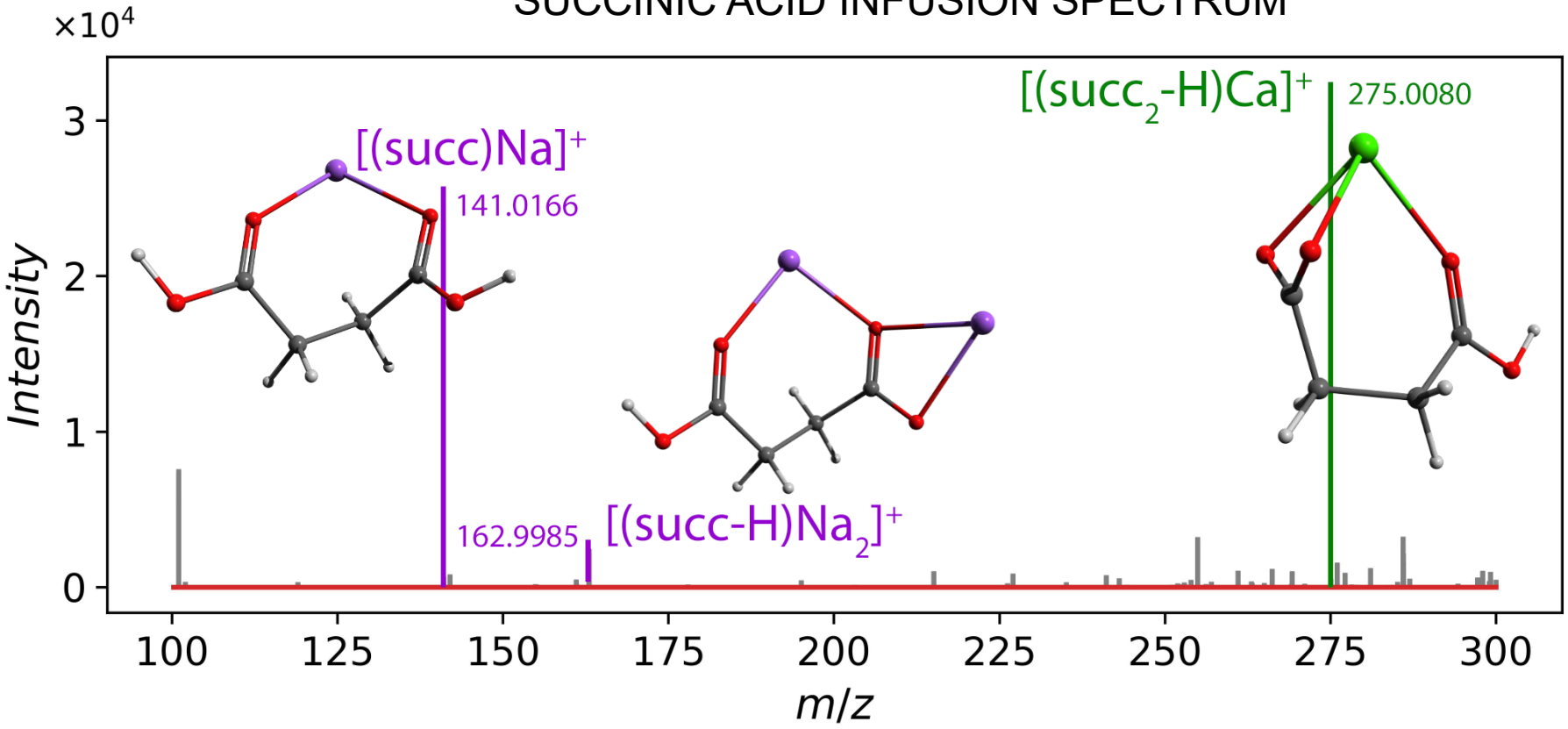
Ions Sampled Into Vacuum



H^+ TRANSFER VS ADDUCT FORMATION

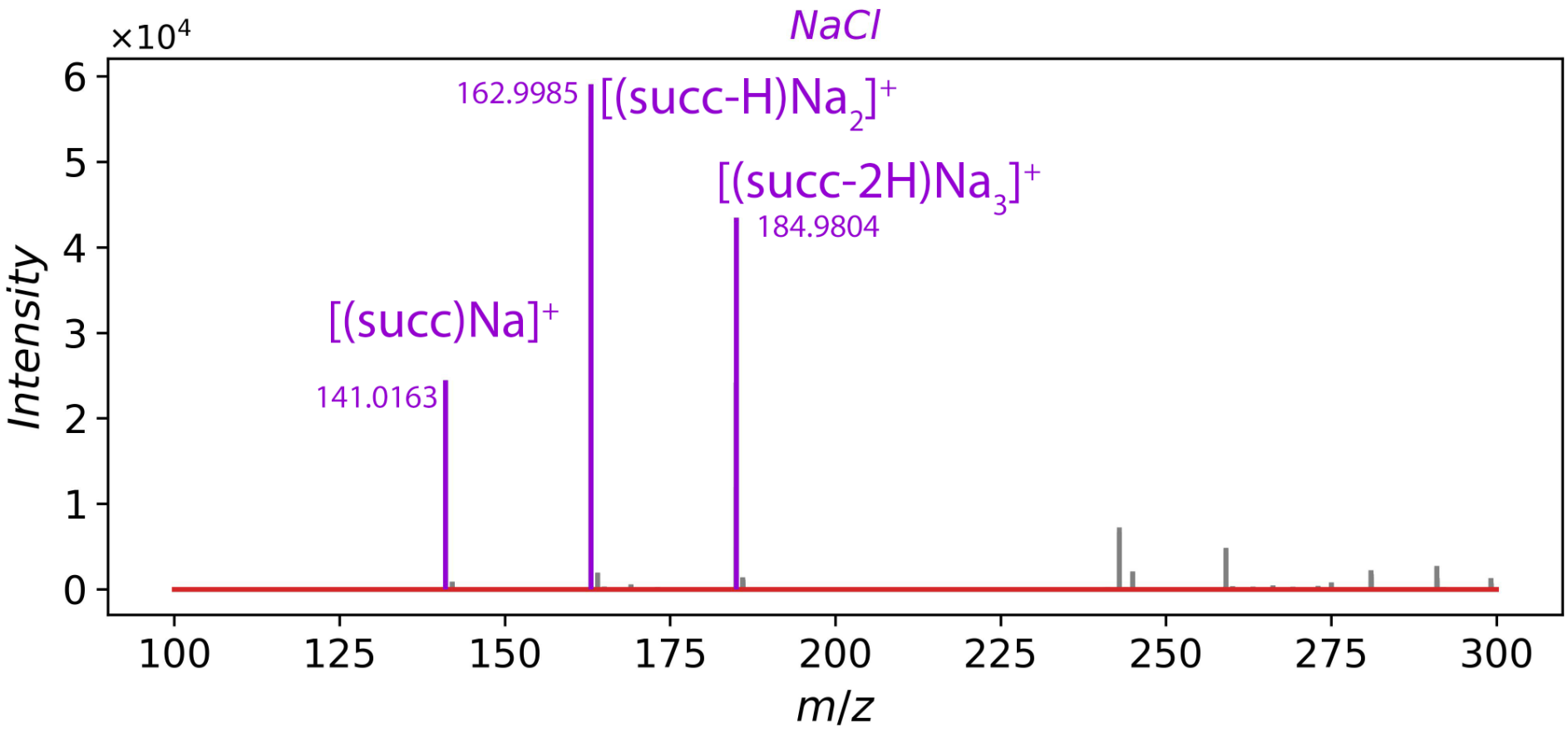


SUCCINIC ACID INFUSION SPECTRUM

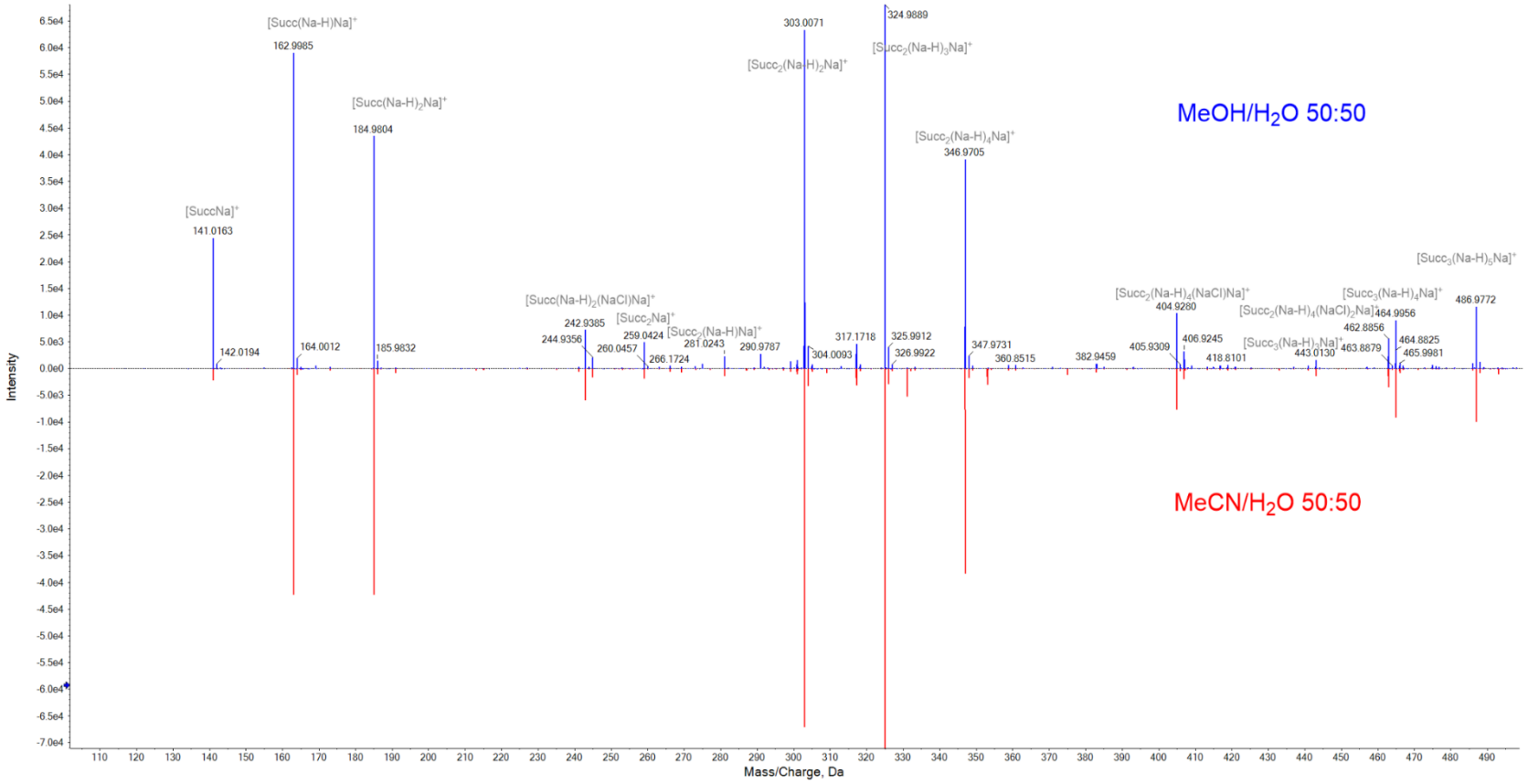


[(succ)H^+] is not present

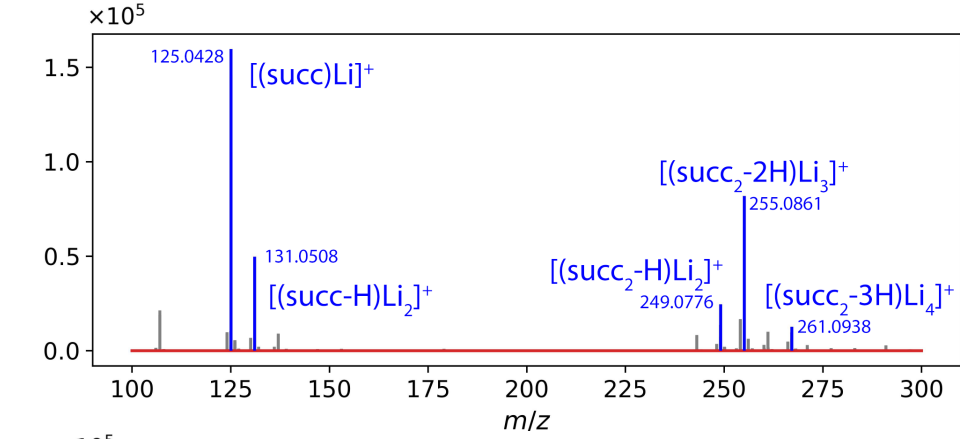
SUCCINIC ACID + 2mM NaCl

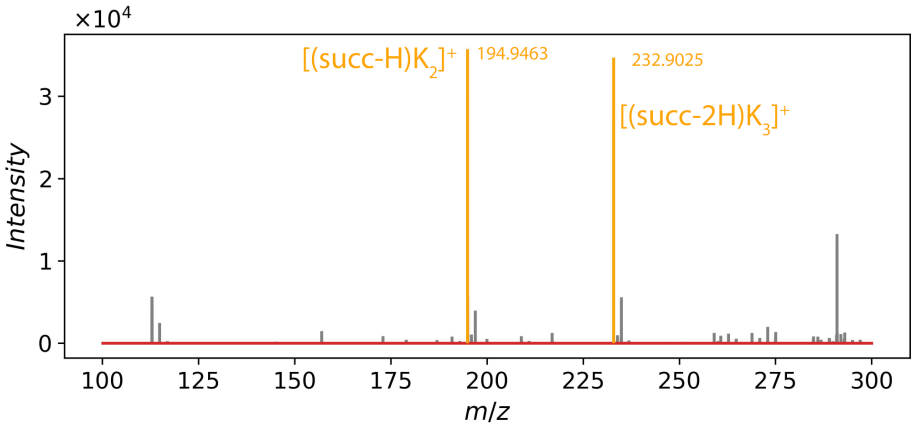


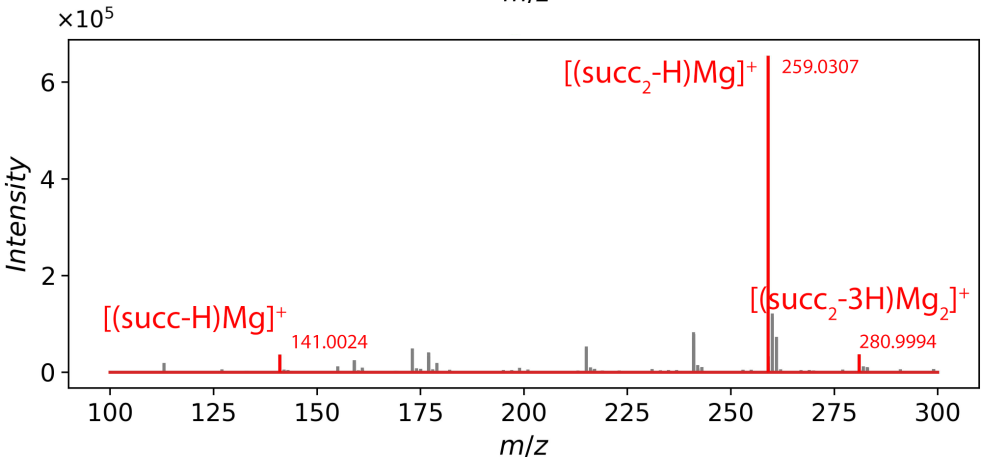
SOLVENT EFFECT: MeCN/H_2O 50% VS MeOH/ H_2O 50%

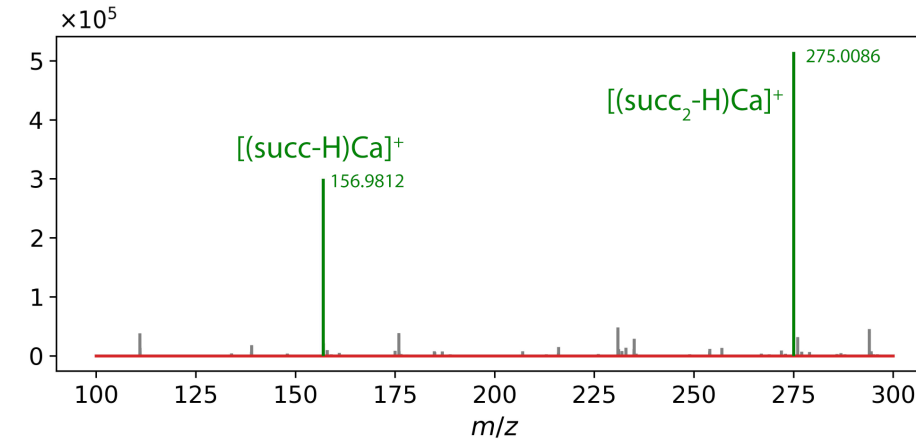


SUCCINIC ACID + 2mM LiCl, KCl, $MgCl_2$ and $CaCl_2$

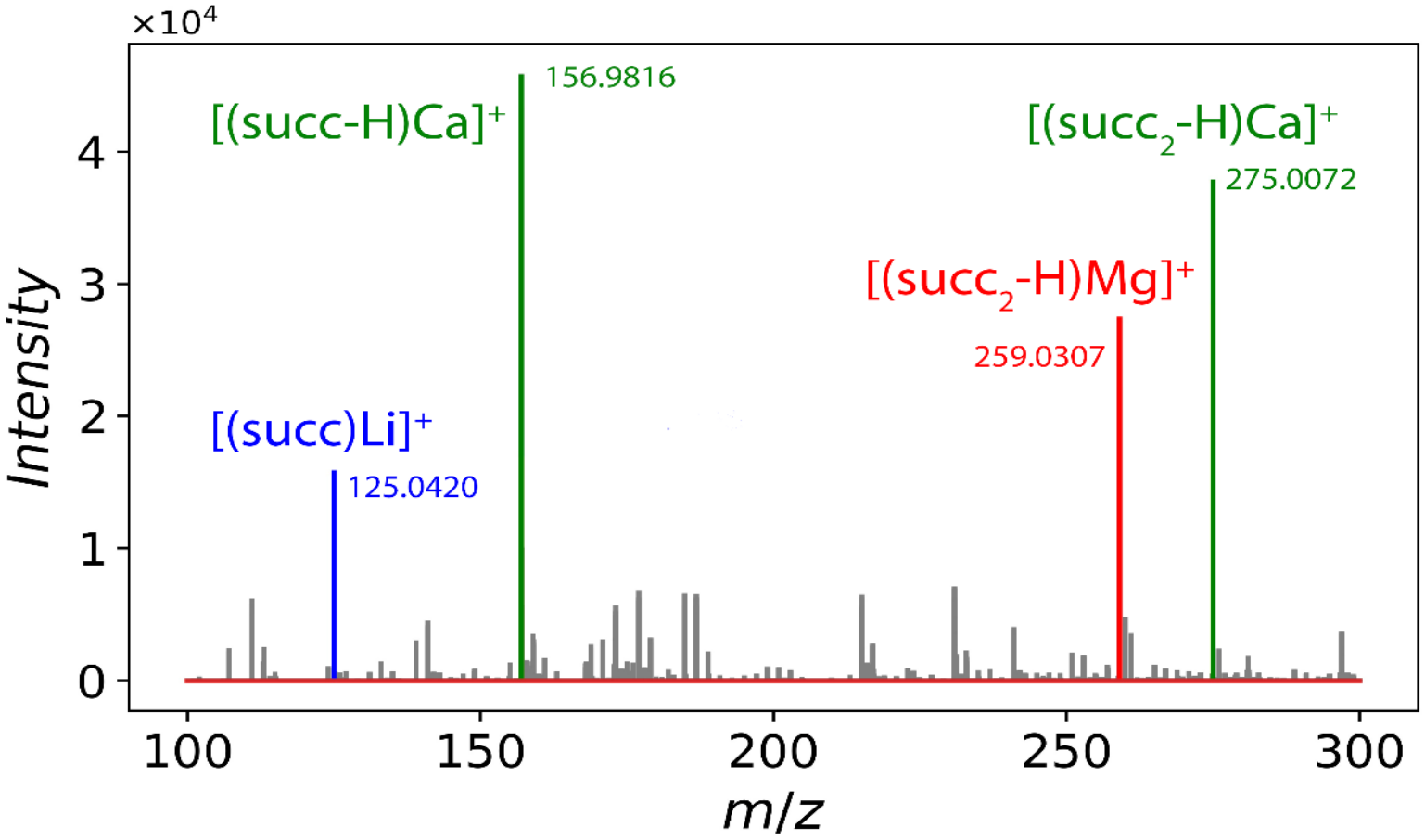








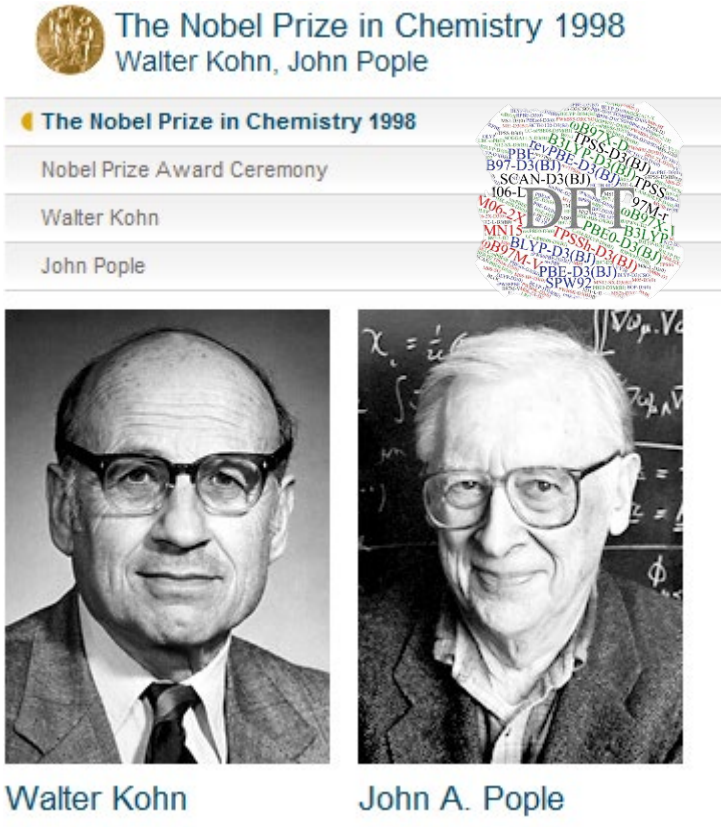
MIXTURE OF LiCl, NaCl, KCl, $MgCl_2$, $CaCl_2$ (c=2mM)



Short introduction to comp. chemistry

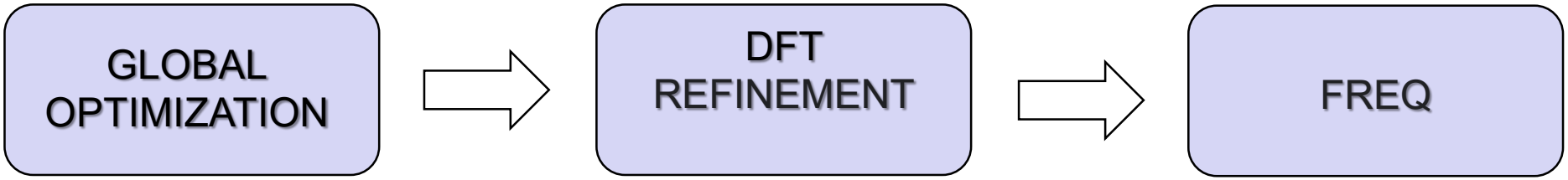
- Empirical methods
- Semiempirical methods
- HF and post-HF methods
  - Ψ based approaches
- DFT
  - ρ based approaches
- Small region of the PES vs MD sampling

Difficulty with EI-MS:
recorded intensity results from complex chemical kinetics and not from energy levels



METHODS

AMS2021



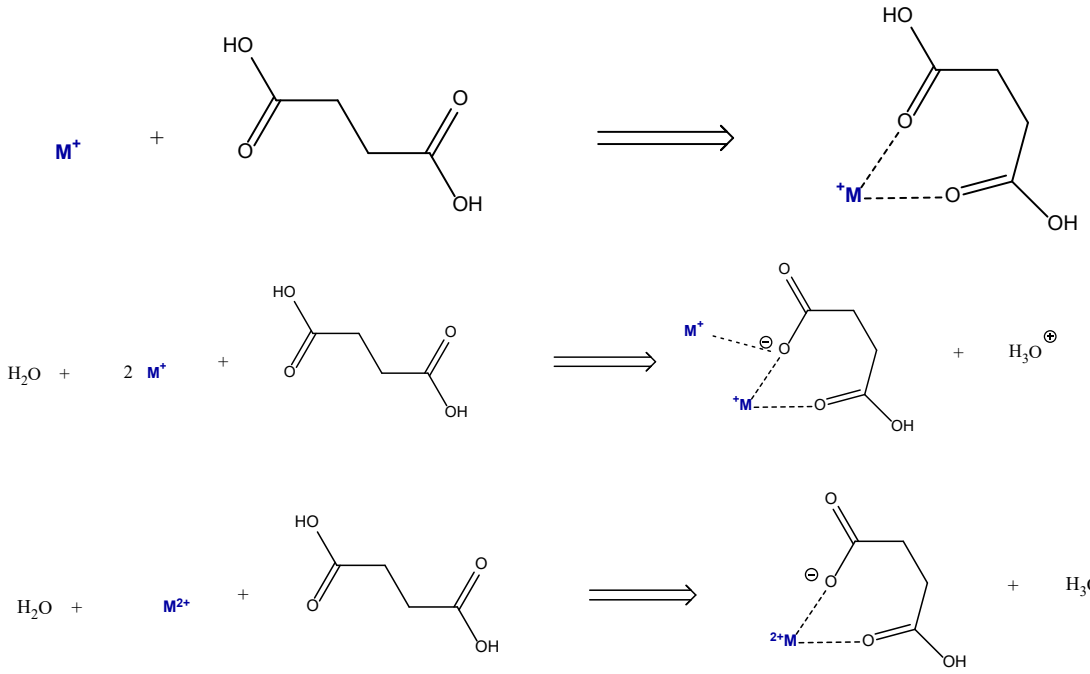
XTB

- Basin Hopping
- systematic variation of dihedrals

PBE (TZ2P)-D4 + COSMO

B3LYP (TZ2P)-D4 + COSMO

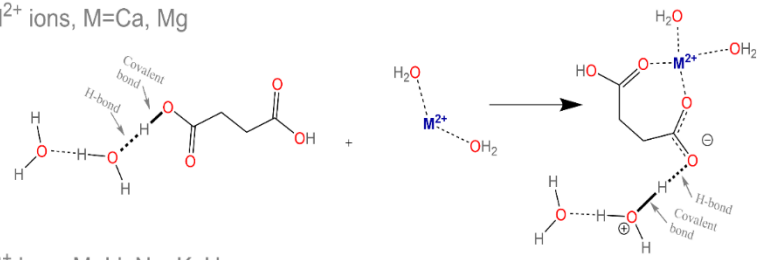
VACUM AND IMPLICIT SOLVATION



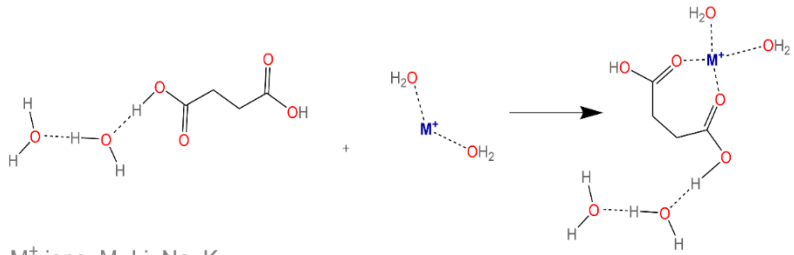
	Vacuum ΔE, PBE	COSMO ΔE, PBE
[(succ-H)·Ca]$^+$	-176.5	-27.9
(succ-H)·Mg]$^+$	-288.8	-56.0
[(succ-H)·2K]$^+$	19.7	12.9
[(succ-H)·2Li]$^+$	-38.9	-22.5
[(succ-H)·2Na]$^+$	-3.1	2.1
[succ·H]$^+$	-44.7	-12.6
[succ·K]$^+$	-32.2	-11.1
[succ·Li]$^+$	-63.5	-32.4
[succ·Na]$^+$	-43.7	-16.9

EXPLICIT SOLVATION

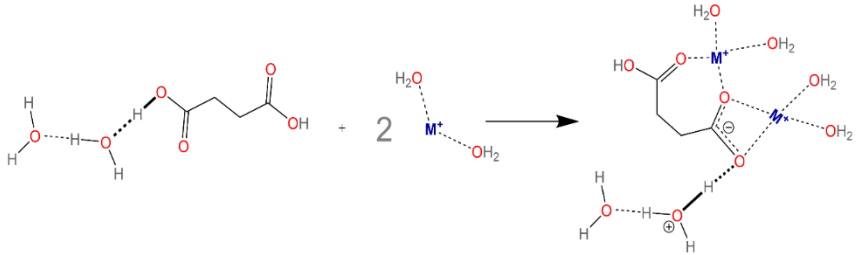
a) M^{2+} ions, M=Ca, Mg



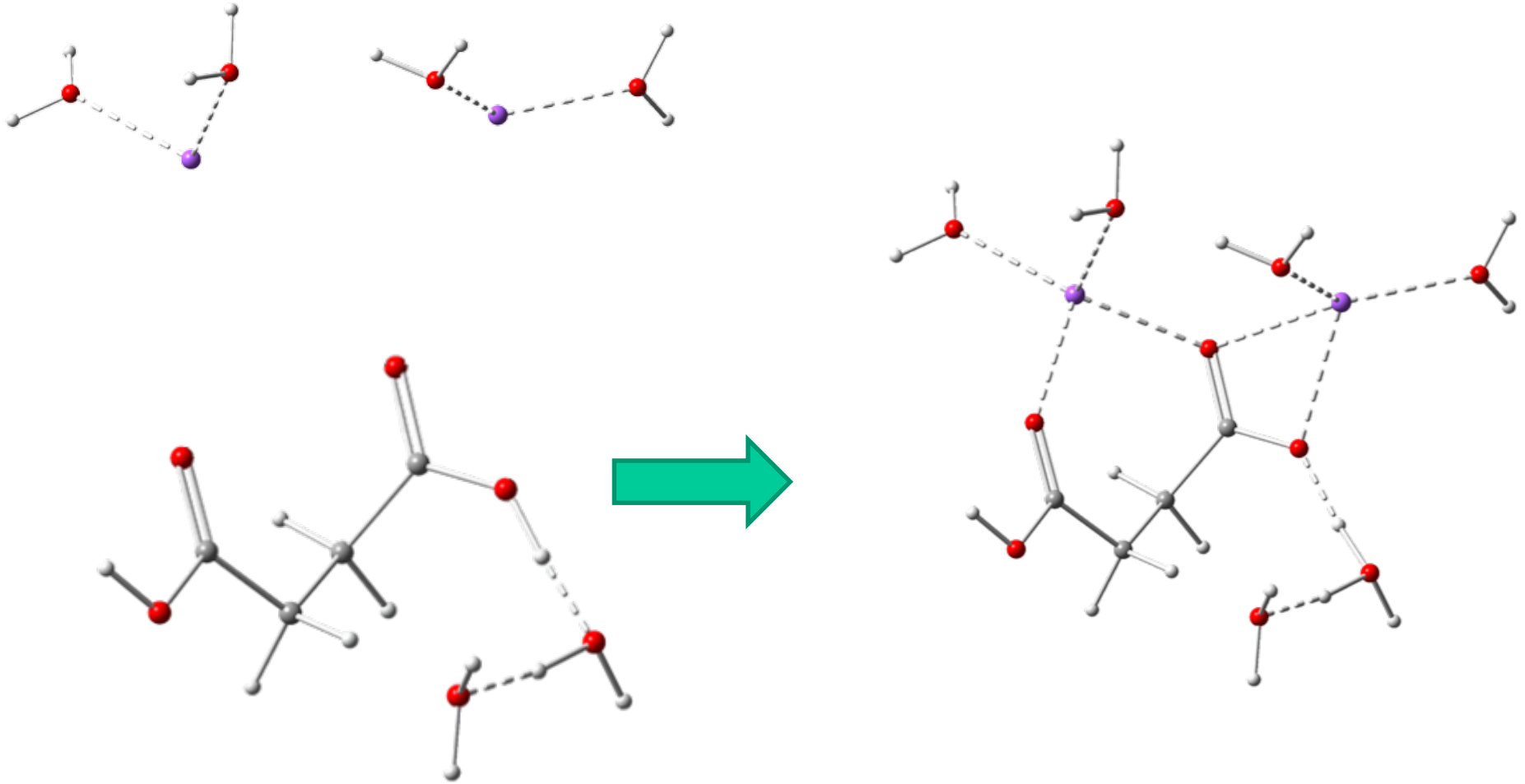
b) M^{+} ions, M=Li, Na, K, H



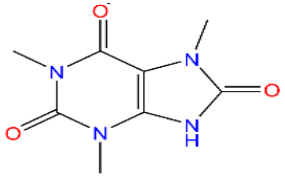
c) M^{+} ions, M=Li, Na, K



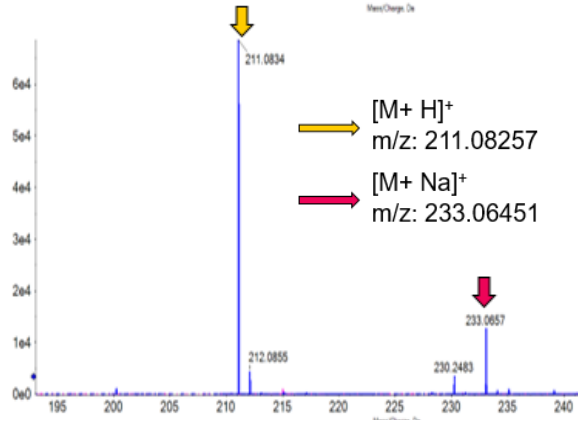
	ΔG PBE	ΔG B3LYP
[(succ-H)·Ca]$^{+}$	-18.1	-17.0
(succ-H)·Mg]$^{+}$	-30.9	-32.1
[(succ-H)·2K]$^{+}$	10.8	12.0
[(succ-H)·2Li]$^{+}$	-16.5	-16.4
[(succ-H)·Na]$^{+}$	-2.8	-3.2
[succ·H]$^{+}$	-0.3	1.9
[succ·K]$^{+}$	6.3	6.4
[succ·Li]$^{+}$	-7.9	-8.4
[succ·Na]$^{+}$	0.2	0.4

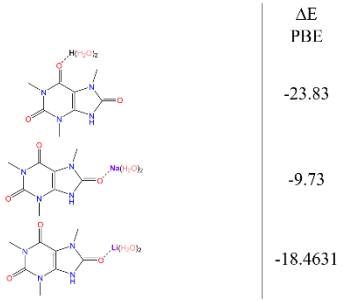


ADITIONAL EXAMPLES

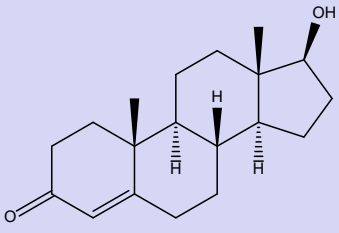


1,3,7 trimethyl uric acid

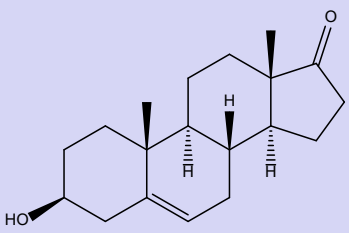




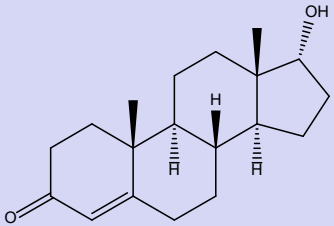
	ΔE PBE
	-23.83
	-9.73
	-18.4631



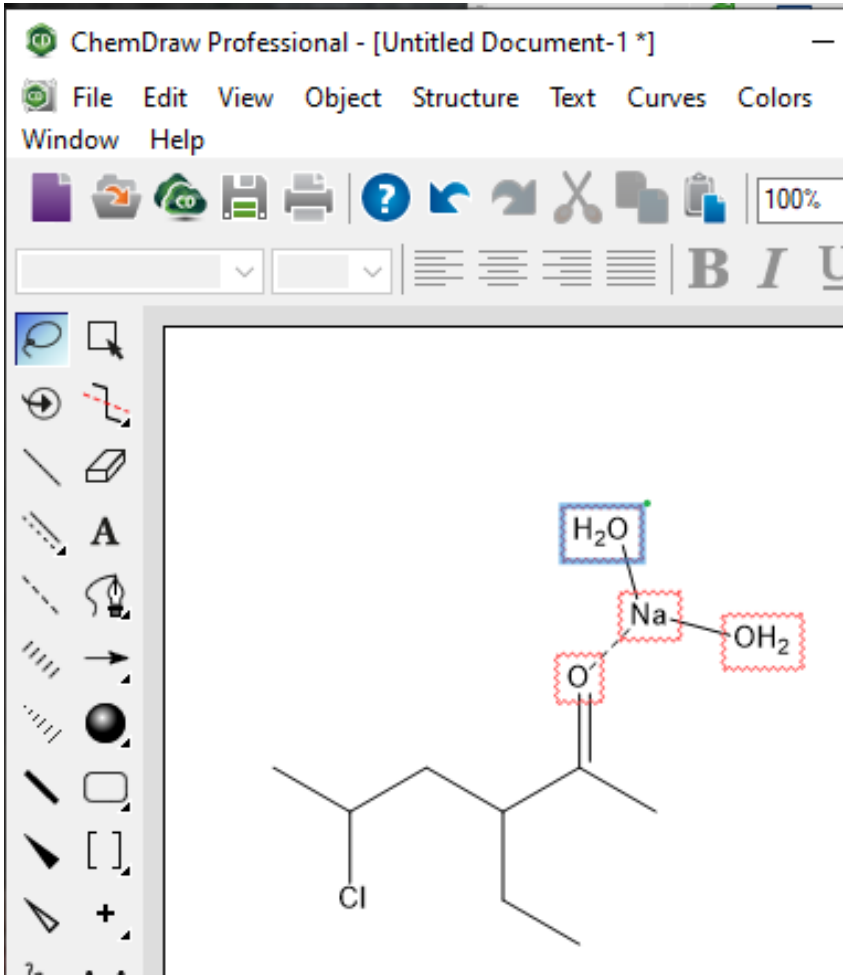
Testosterone



Epitestosterone



Dehydroepiandrosterone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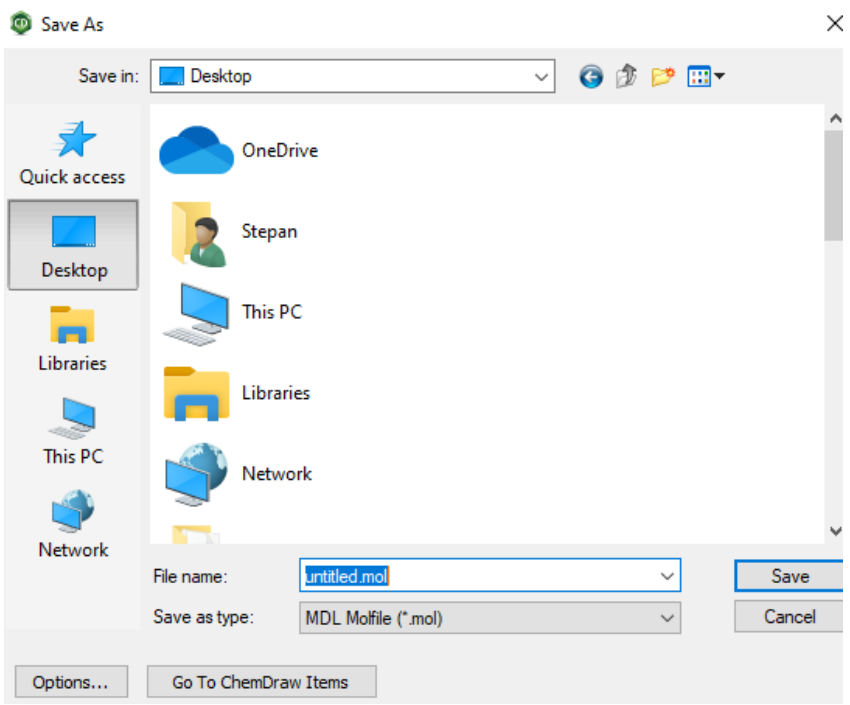
File Edit View Object Structure Text Curves Colors
Window Help
100%
H2O
Na
OH2
O
Cl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Save in: Desktop
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Save
Cancel
Options...
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Conclusions

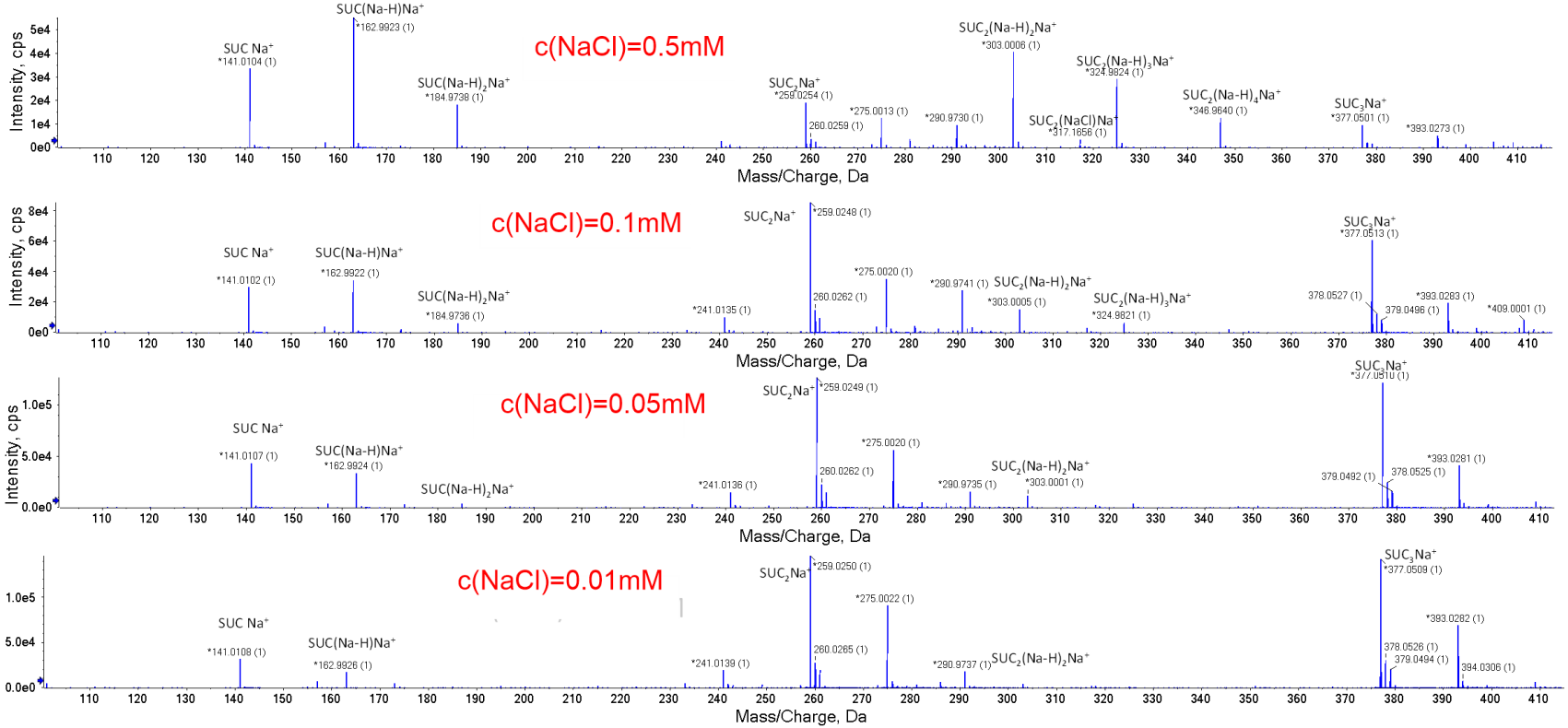
ΔG estimation using explicitly solvated interaction center and DFT.

1) The model is applied on succinic acid but it is simple and easily extendable procedure

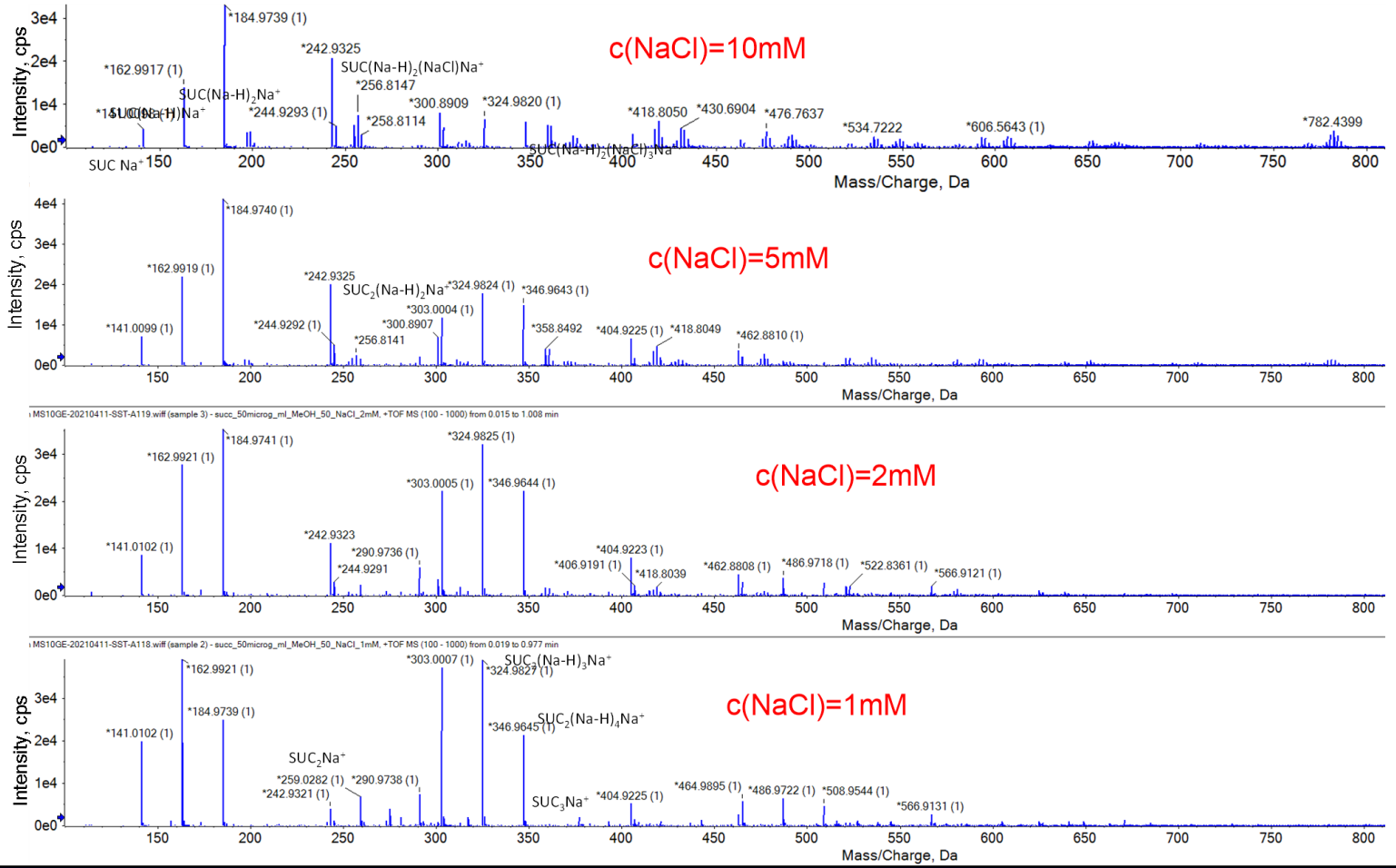
2) Simple thermodynamics of protonation/adduct formation correlates nicely with ionization efficiency

3) M^{2+} ion adducts should no longer be neglected, especially when analytes possess strongly coordinating functional groups.

EFFECT OF VARYING THE NaCl CONCENTRATION

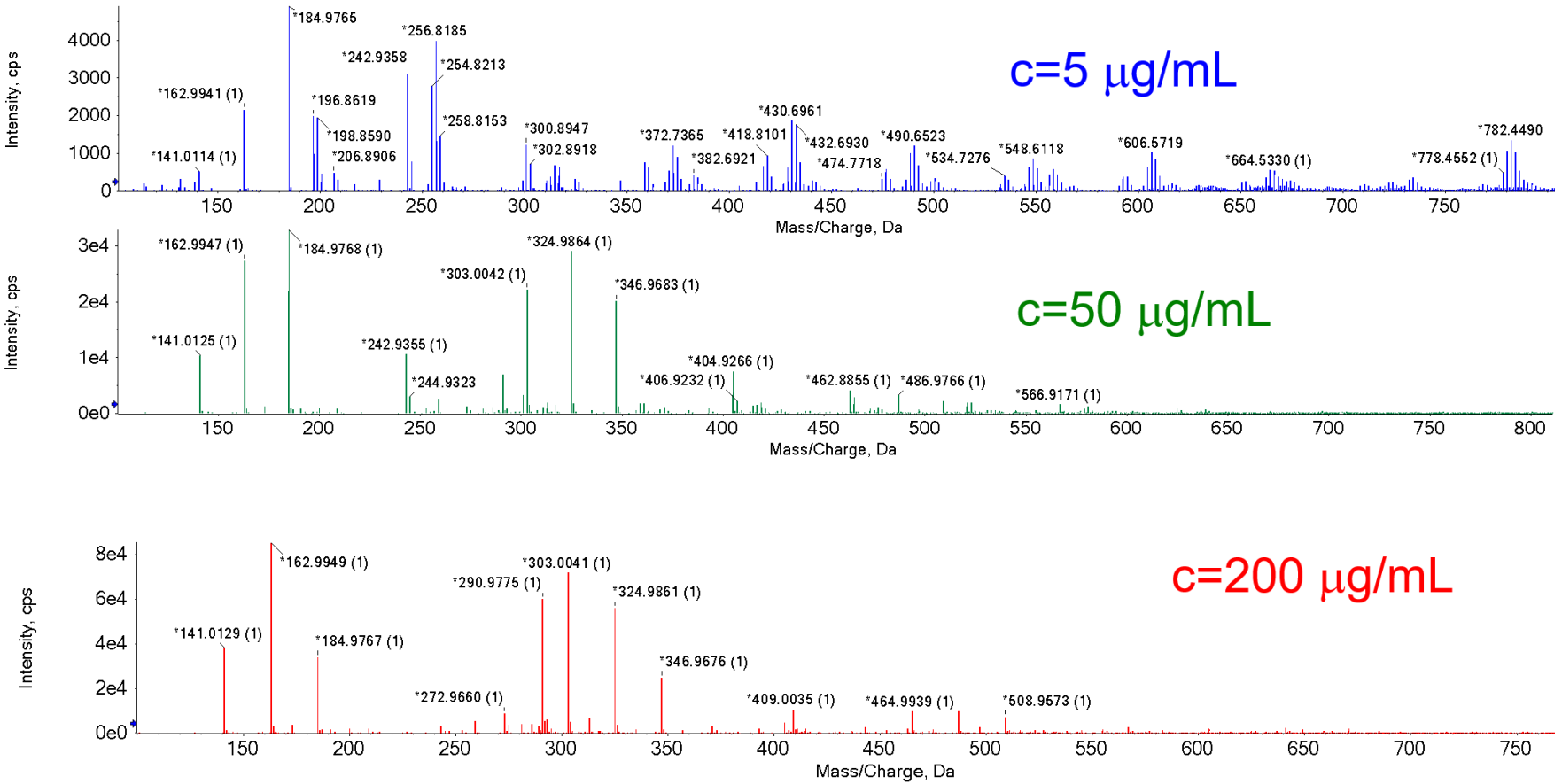


EFFECT OF VARYING THE NaCl CONCENTRATION

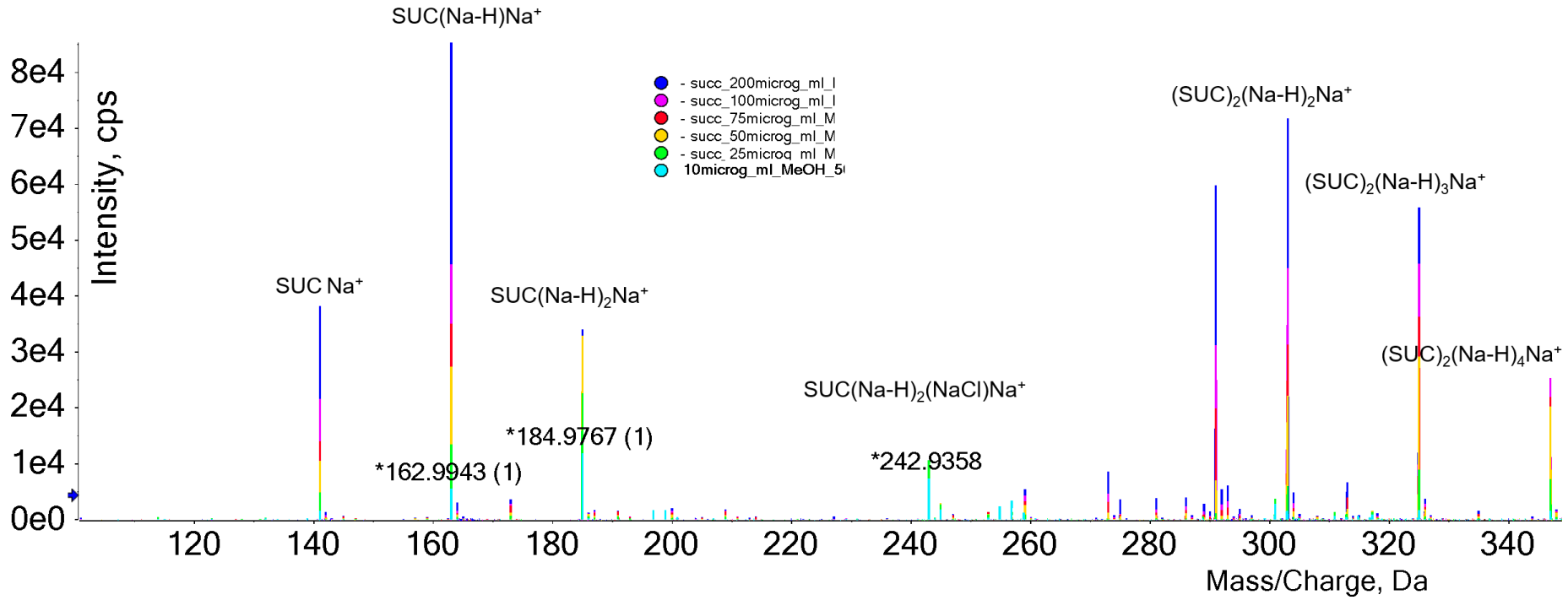


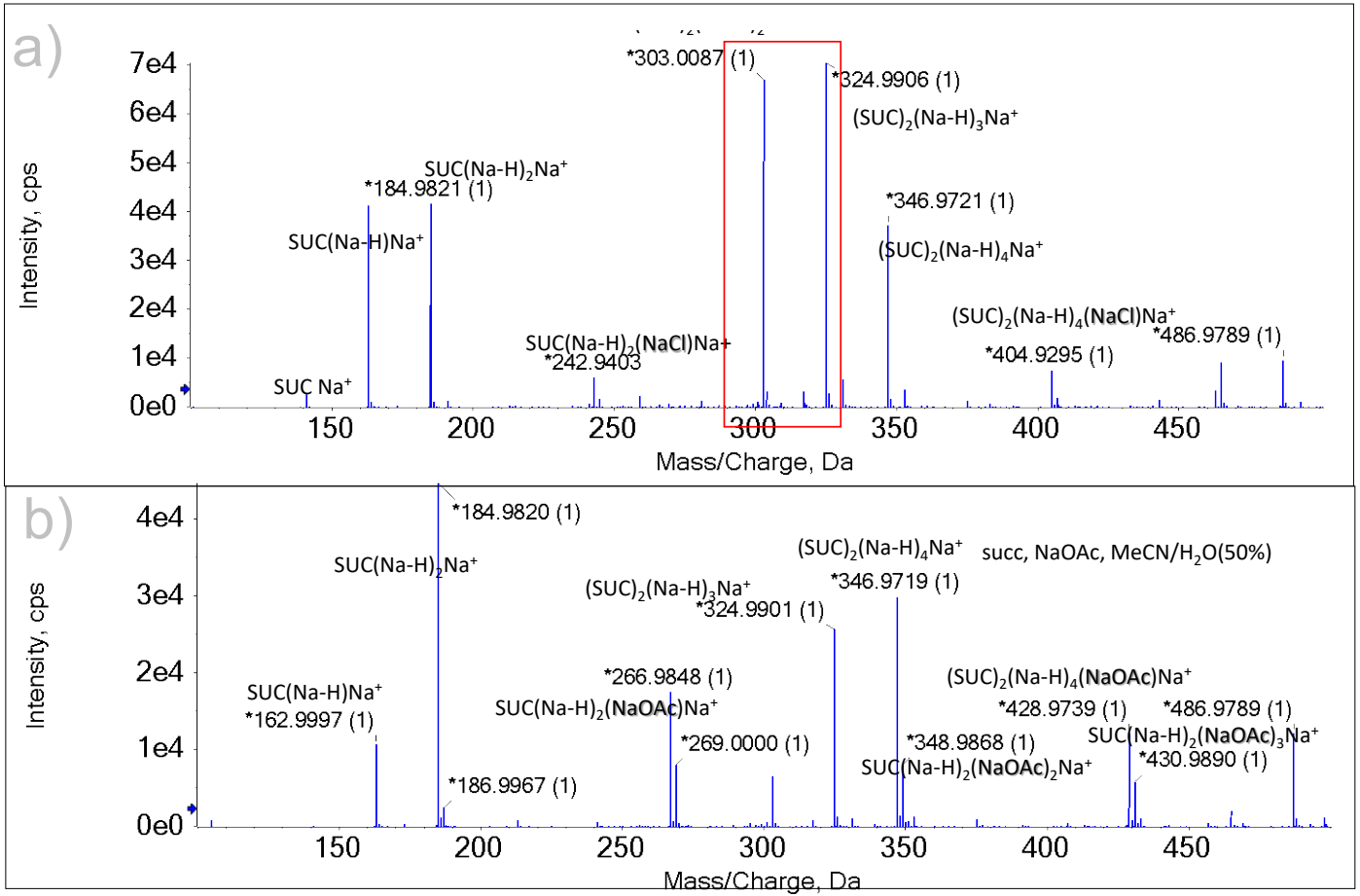
succ =100µg/mLMeOH/H_2O(50%)

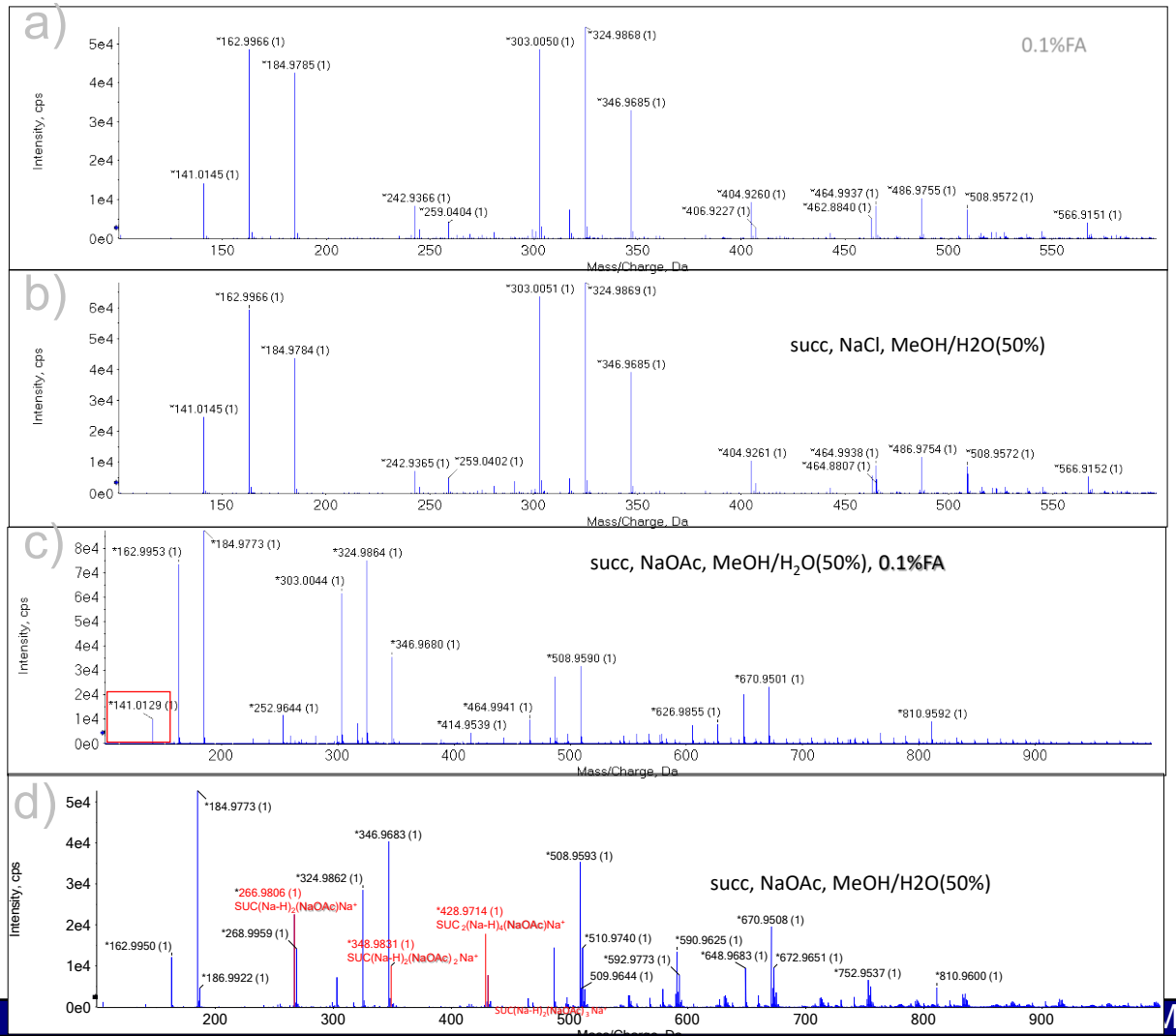
SUCCINIC ACID CONC IS VARIED, C(NACl)= 2mM, MEOH/H_2O(50%)

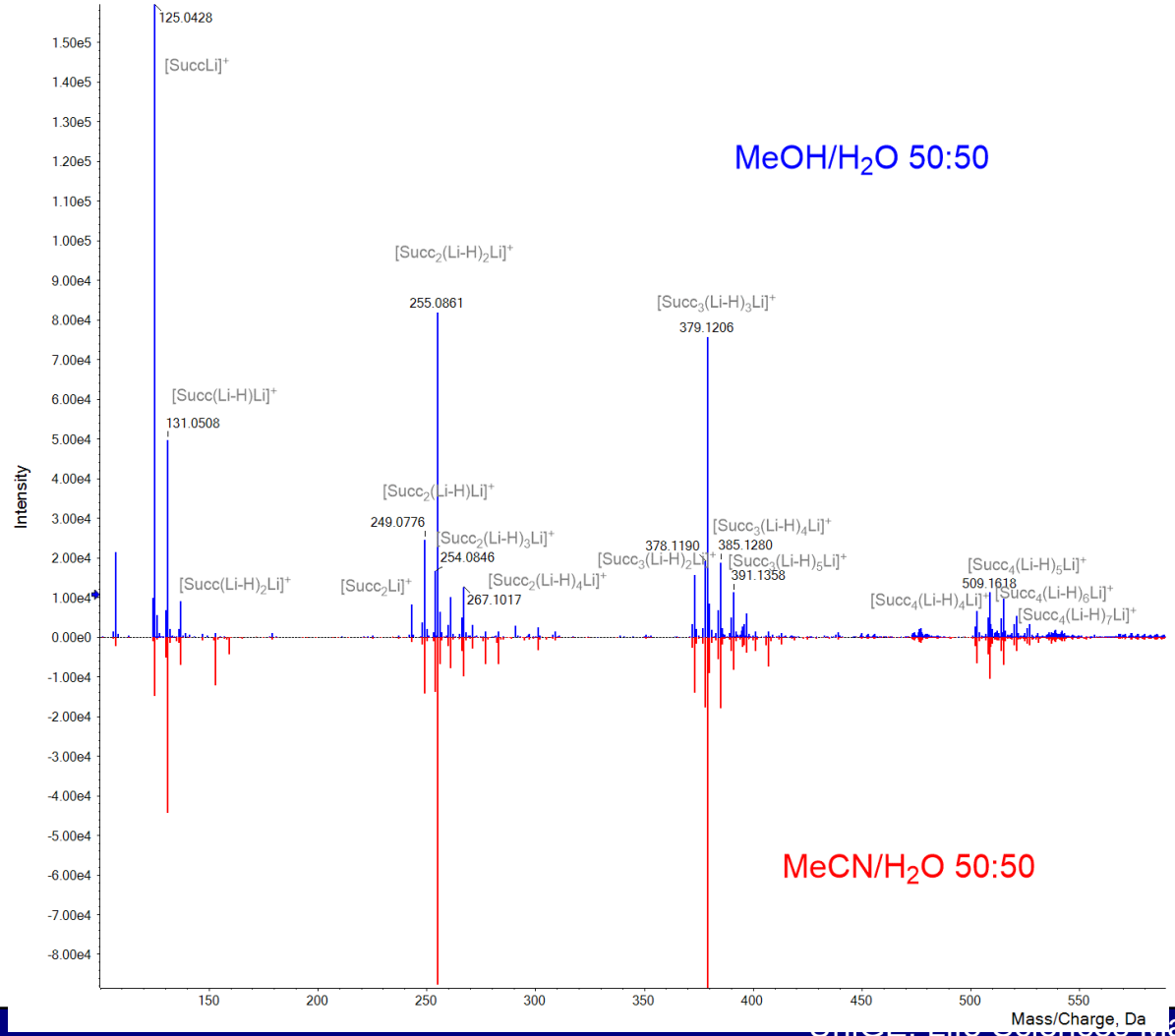


SUCCINIC ACID CONC IS VARIED, C(NACl)= 2mM, MEOH/H_2O(50%)




a)
Intensity, cps
7e4
6e4
5e4
4e4
3e4
2e4
1e4
0e0
*303.0087 (1)
*324.9906 (1)
(SUC)2(Na-H)3Na+
SUC(Na-H)2Na+
*184.9821 (1)
*346.9721 (1)
SUC(Na-H)Na+
(SUC)2(Na-H)4Na+
(SUC)2(Na-H)4(NaCl)Na+
*486.9789 (1)
SUC(Na-H)2(NaCl)Na+
*242.9403
*404.9295 (1)
SUC Na+
150
200
250
300
350
400
450
Mass/Charge, Da
b)
Intensity, cps
4e4
3e4
2e4
1e4
0e0
*184.9820 (1)
SUC(Na-H)2Na+
(SUC)2(Na-H)4Na+
succ, NaOAc, MeCN/H2O(50%)
*346.9719 (1)
(SUC)2(Na-H)3Na+
*324.9901 (1)
*266.9848 (1)
(SUC)2(Na-H)4(NaOAc)Na+
SUC(Na-H)Na+
*162.9997 (1)
SUC(Na-H)2(NaOAc)Na+
*428.9739 (1)
*486.9789 (1)
*269.0000 (1)
*348.9868 (1)
SUC(Na-H)2(NaOAc)3Na+
*430.9890 (1)
SUC(Na-H)2(NaOAc)2Na+
*186.9967 (1)
150
200
250
300
350
400
450
Mass/Charge, Da


a)
0.1%FA
Intensity, cps
Mass/Charge, Da
b)
succ, NaCl, MeOH/H2O(50%)
Intensity, cps
Mass/Charge, Da
c)
succ, NaOAc, MeOH/H2O(50%), 0.1%FA
Intensity, cps
Mass/Charge, Da
d)
succ, NaOAc, MeOH/H2O(50%)
Intensity, cps
Mass/Charge, Da


125.0428
[SuccLi]+
MeOH/H2O 50:50
[Succ2(Li-H)2Li]+
255.0861
[Succ3(Li-H)3Li]+
379.1206
[Succ(Li-H)Li]+
131.0508
[Succ2(Li-H)Li]+
249.0776
[Succ2(Li-H)3Li]+
254.0846
[Succ3(Li-H)4Li]+
385.1280
378.1190
[Succ3(Li-H)2Li]+
[Succ3(Li-H)5Li]+
391.1358
[Succ4(Li-H)5Li]+
509.1618
[Succ4(Li-H)6Li]+
[Succ4(Li-H)7Li]+
[Succ(Li-H)2Li]+
[Succ2Li]+
[Succ2(Li-H)4Li]+
267.1017
[Succ4(Li-H)4Li]+
MeCN/H2O 50:50
Intensity
1.50e5
1.40e5
1.30e5
1.20e5
1.10e5
1.00e5
9.00e4
8.00e4
7.00e4
6.00e4
5.00e4
4.00e4
3.00e4
2.00e4
1.00e4
0.00e0
-1.00e4
-2.00e4
-3.00e4
-4.00e4
-5.00e4
-6.00e4
-7.00e4
-8.00e4
150
200
250
300
350
400
450
500
550
Mass/Charge, Da

Thank you for your attention!

Questions?