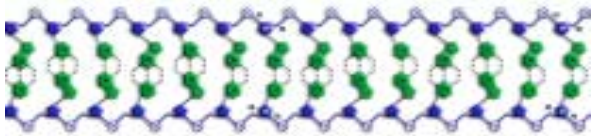

Metabolon

Organization

- Metabolomics overview
- Methodologies
- Case studies

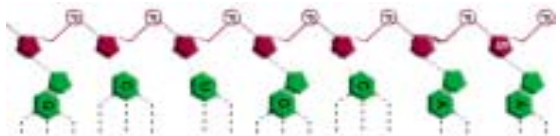
Metabolomics

DNA



Genomics – 25,000 Genes

RNA

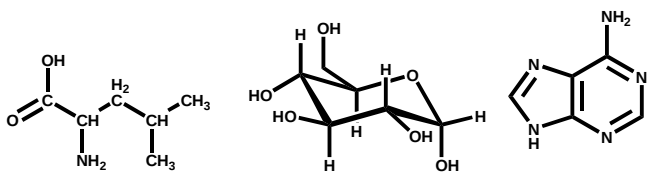


Transcriptomics – 100,000 Transcripts

Protein

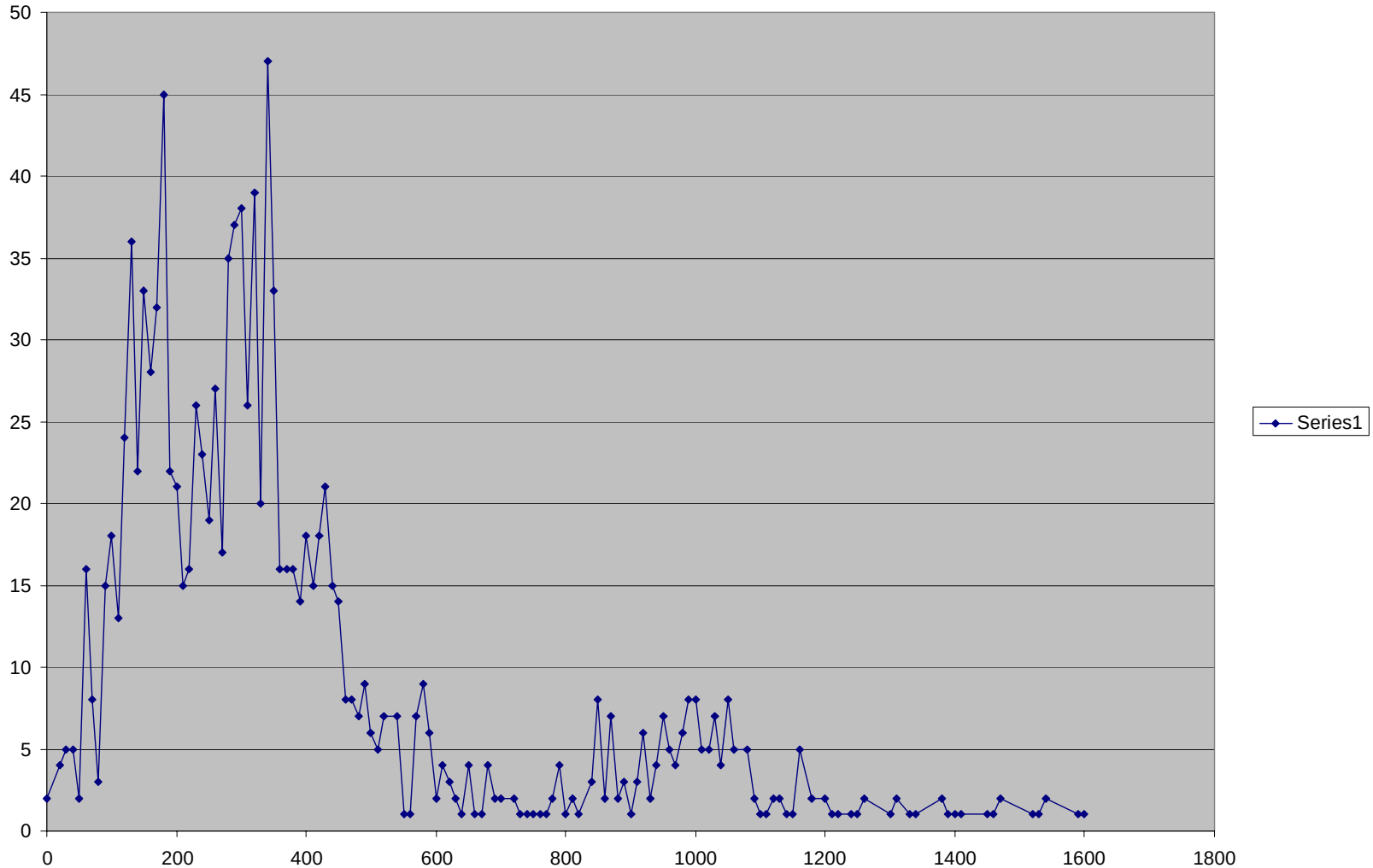
Proteomics – 1,000,000 Proteins

Biochemicals (Metabolites)



Metabolomics – 2,400 Compounds

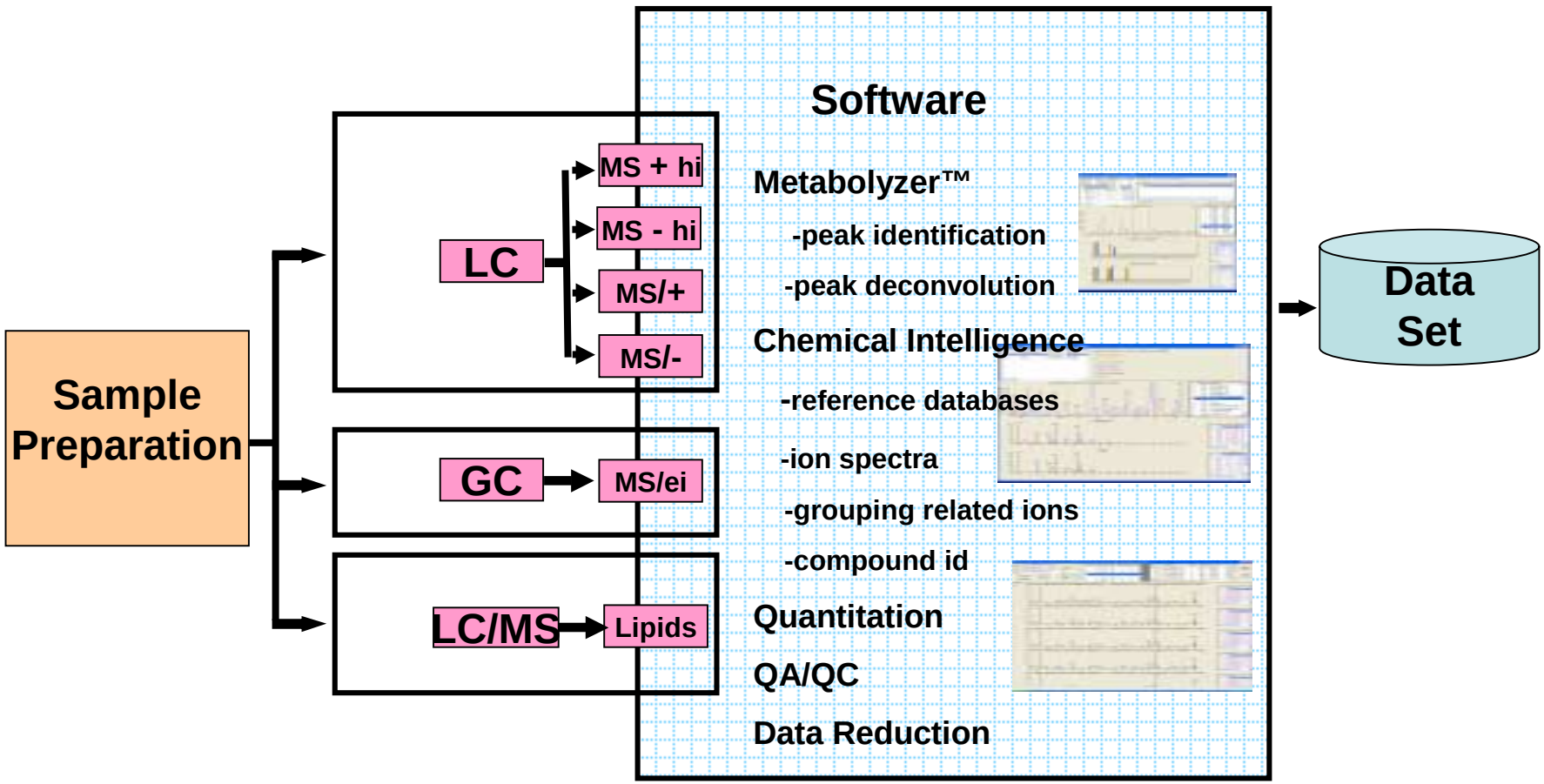
Mass Distributions in the Human Metabolome



Benefits

- Precise
- Quantitative
- Relevant
- Less Complex

Metabolon Process Overview



Sample Preparation

Sample Preparation

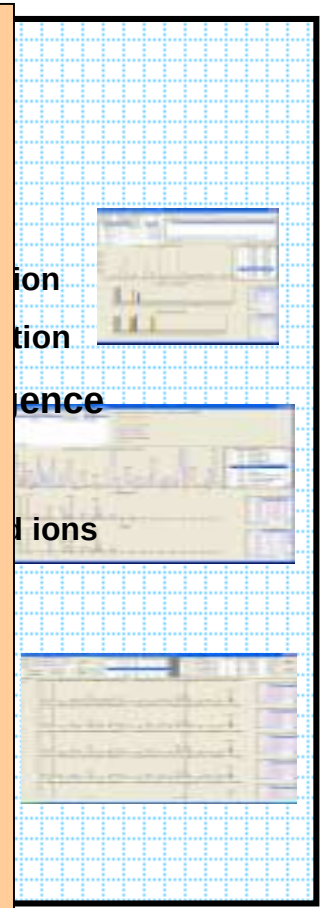
Complete extraction of hydrophobic and hydrophilic molecules

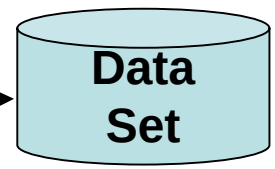
Automated and roboticized

Designed for small molecule isolation

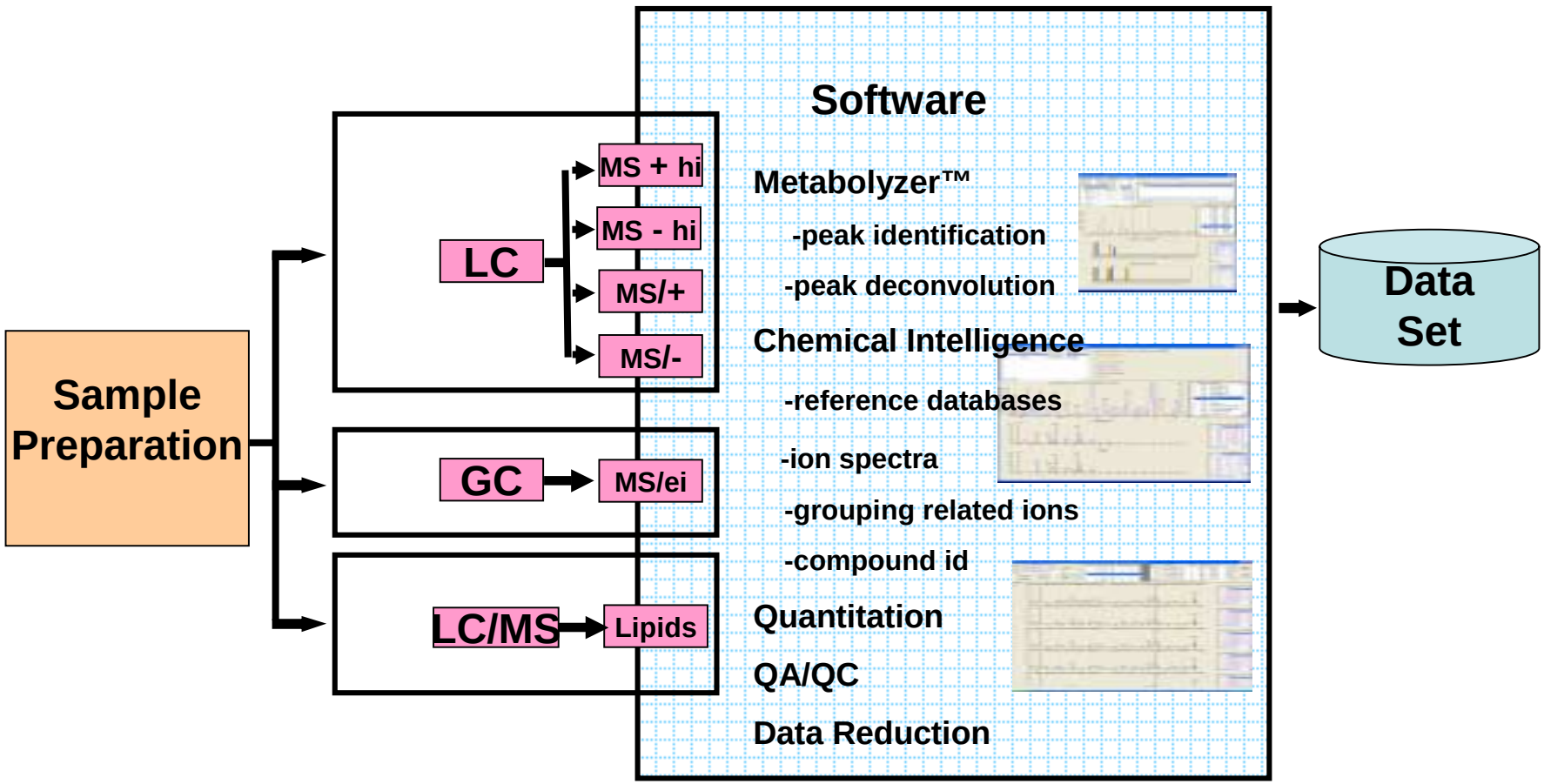
- release small molecules
- ppt protein
- multiple pellet wash

amniotic fluid
breast exudate
CSF
tissues
plasma
cell cultures
E. coli

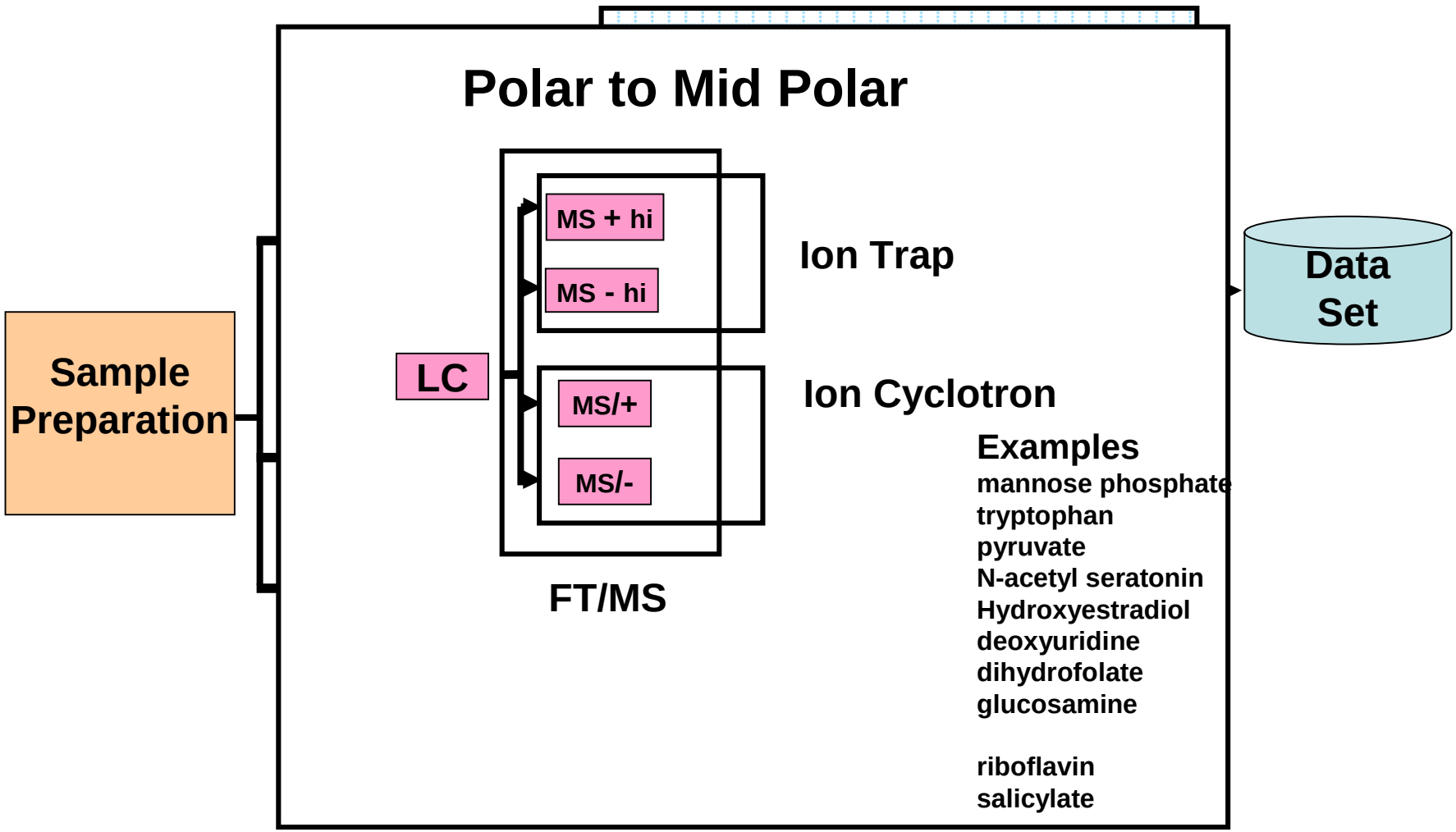




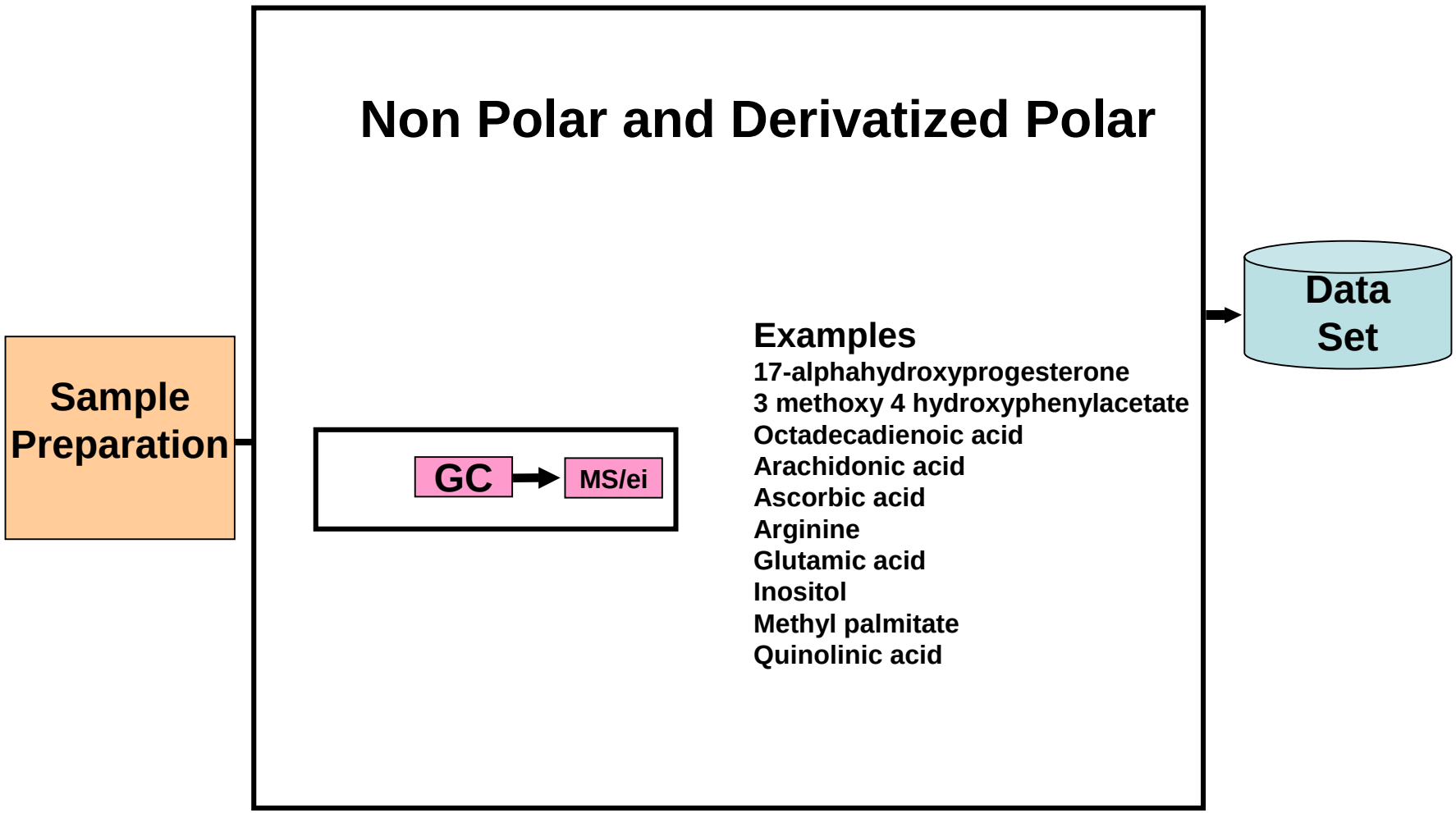
Metabolon Process Overview



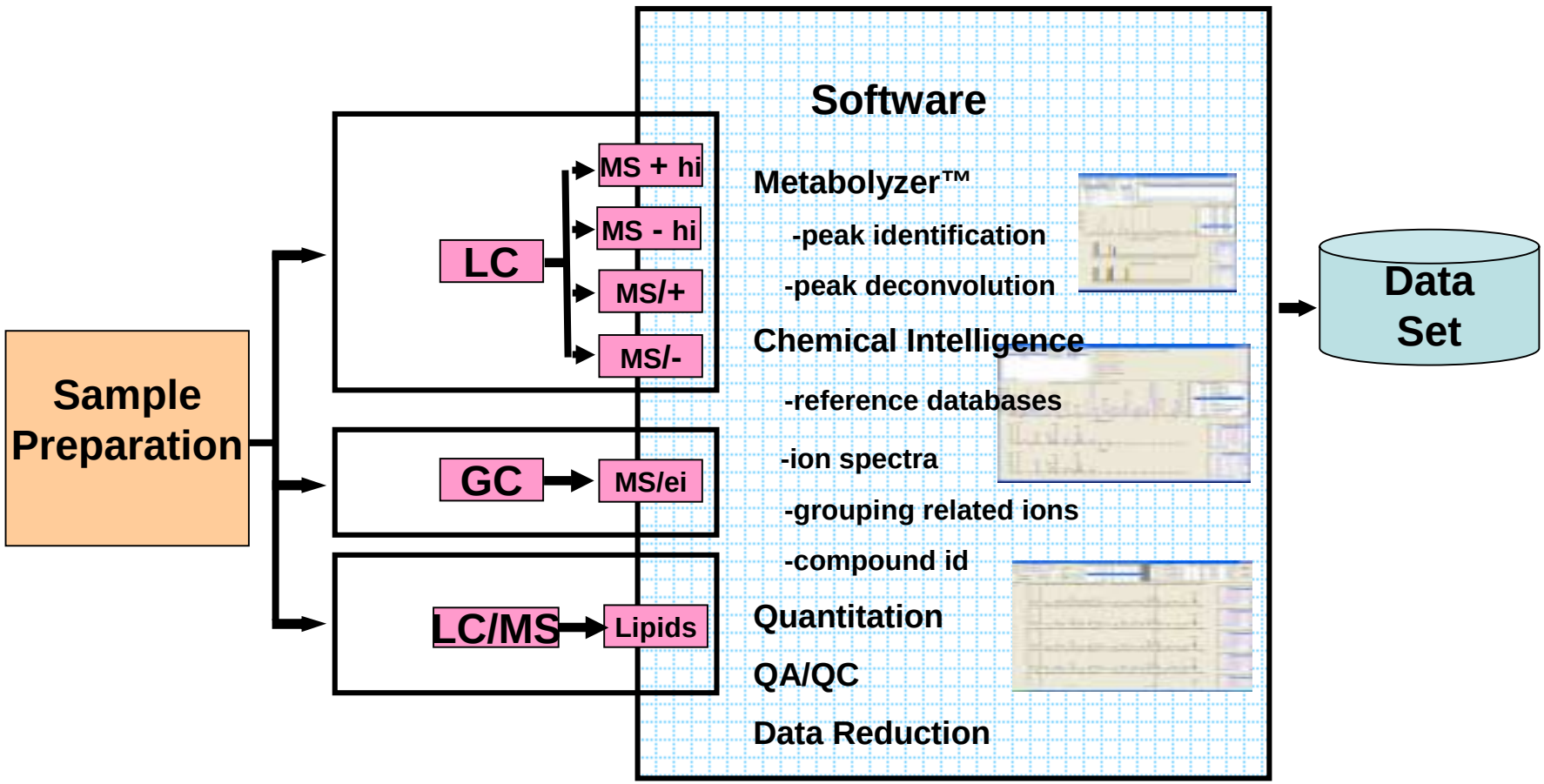
LC processes



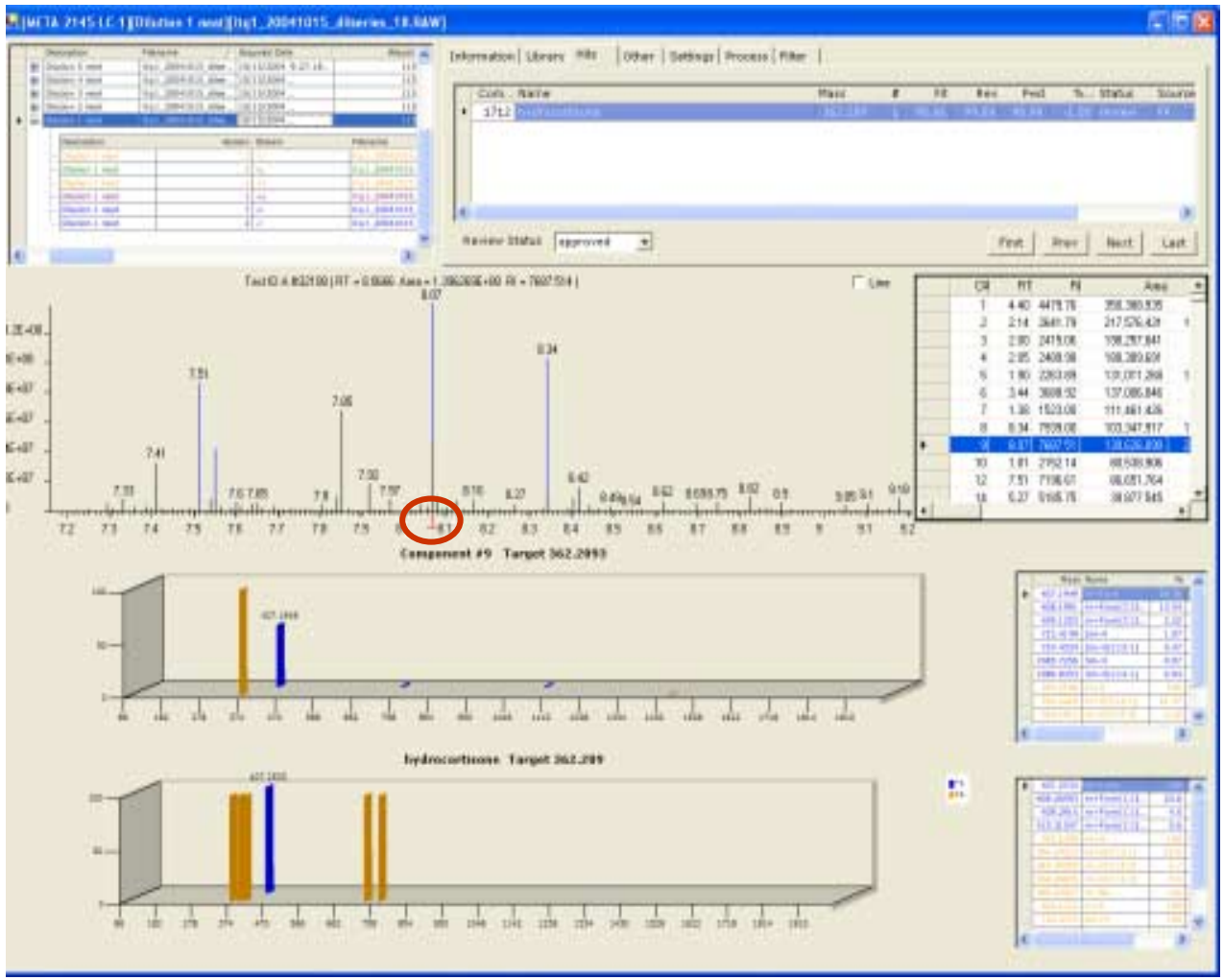
GC processes



Software


Sample Preparation
LC
MS + hi
MS - hi
MS/+
MS/-
GC
MS/ei
LC/MS
Lipids
Software
Metabolyzer™
-peak identification
-peak deconvolution
Chemical Intelligence
-reference databases
-ion spectra
-grouping related ions
-compound id
Quantitation
QA/QC
Data Reduction
Data Set

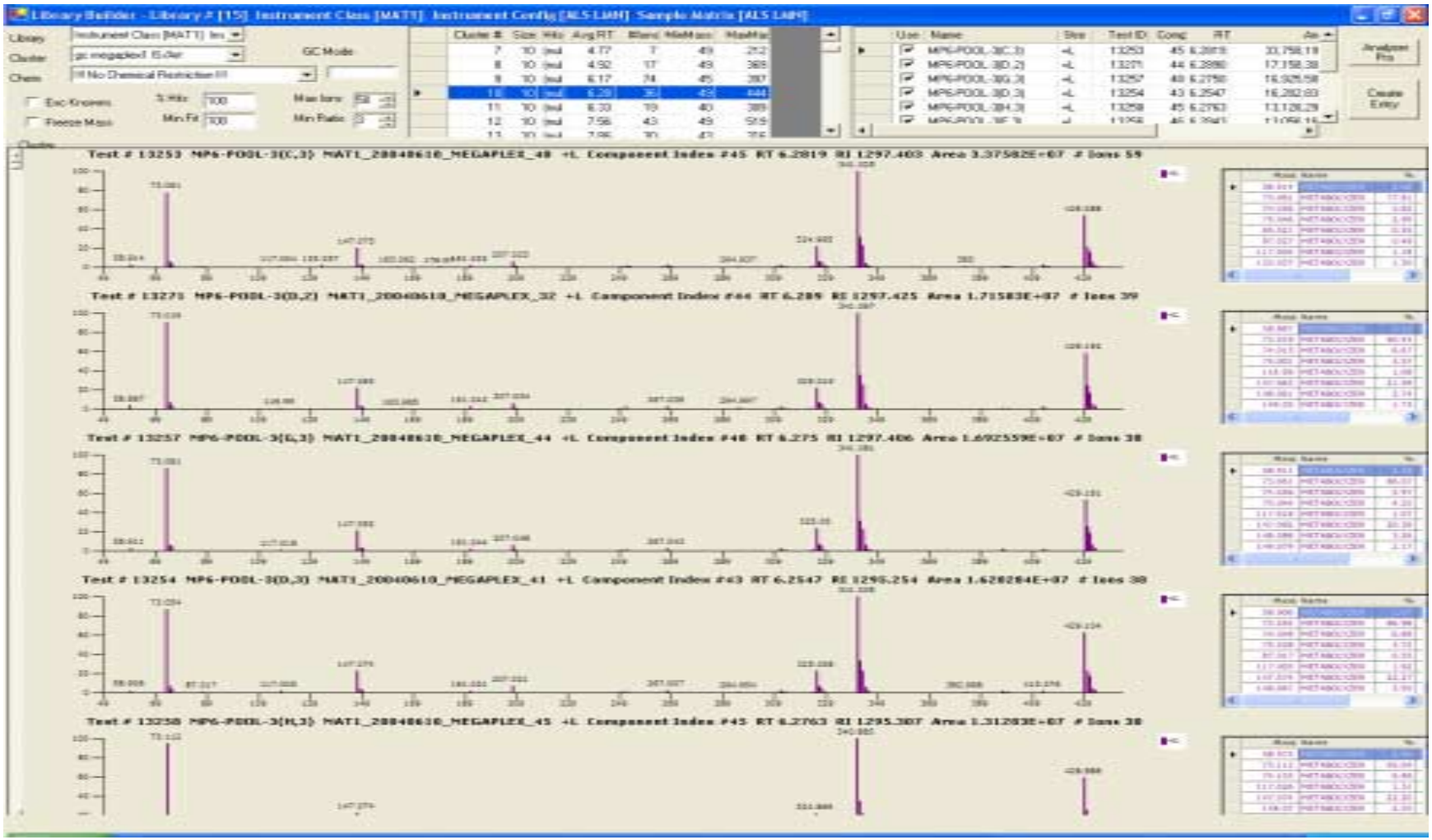
LC Data



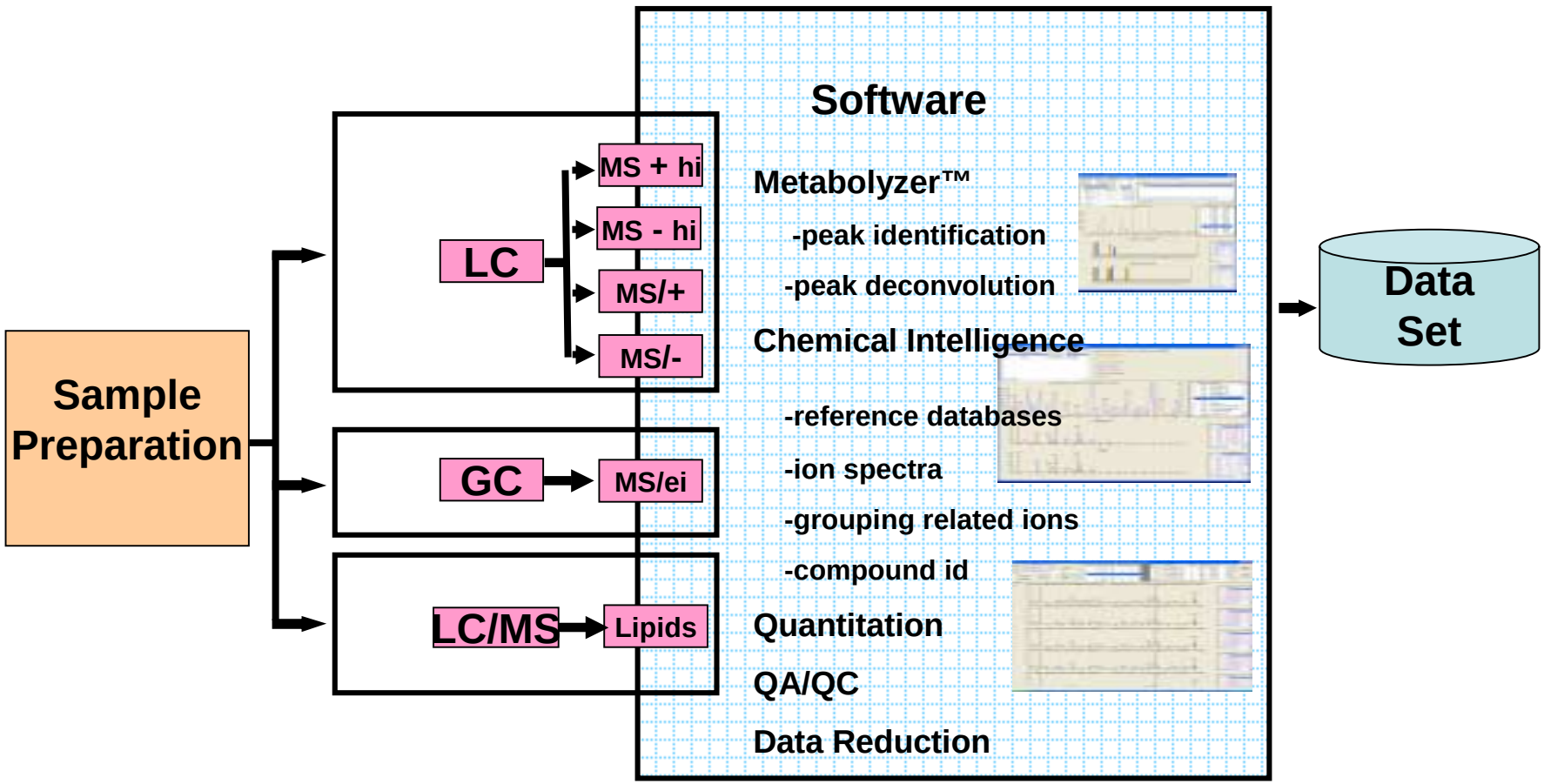
GC Data


Information | Library | Hits | Other | Settings | Process
Instrument Standard
Recovery Standard
Derivitization Standard
Known Compound
Unknown Compound
Unknown Component
Artifact
Component #141
myo-Inositol

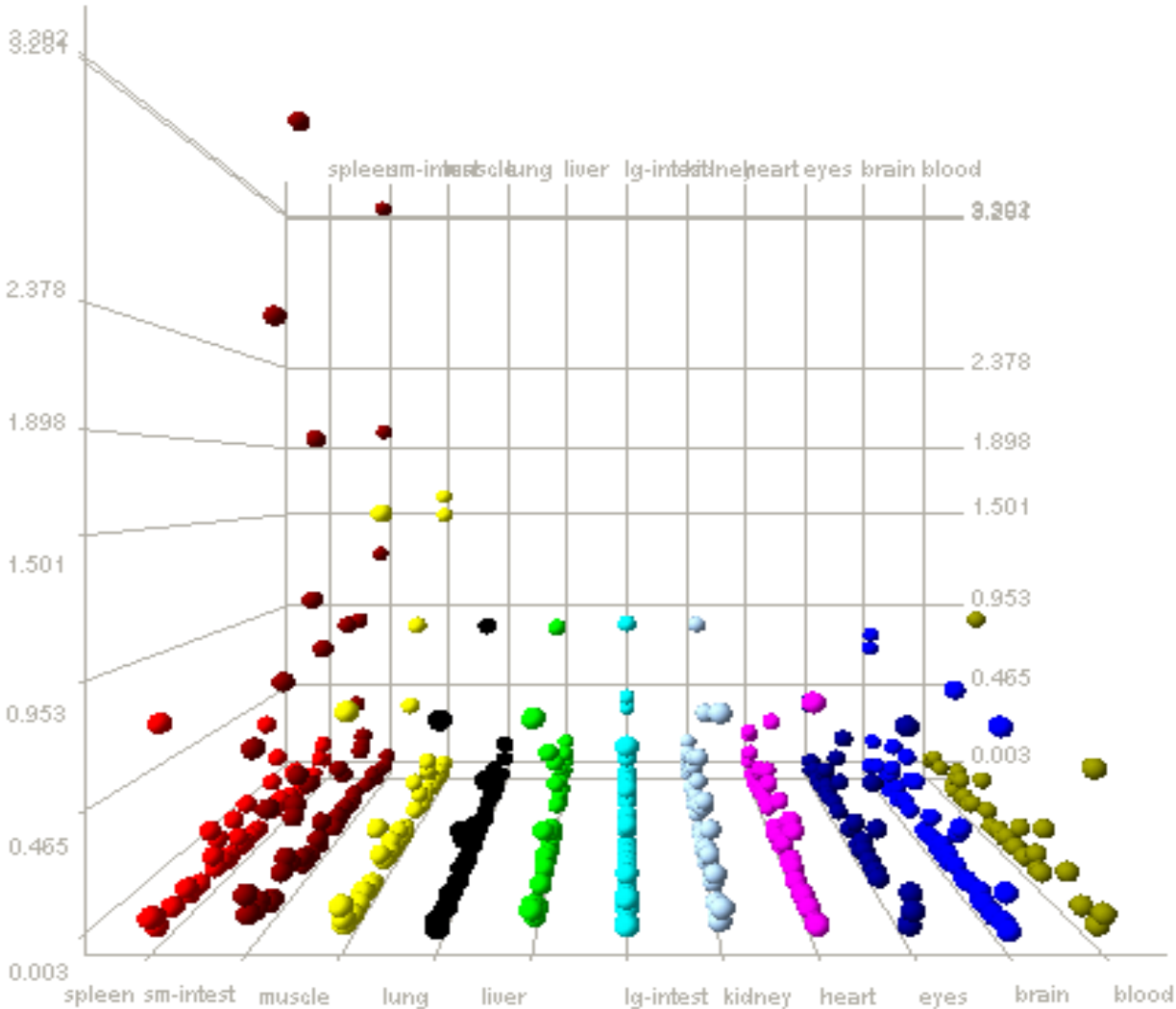
Chemical Library Building



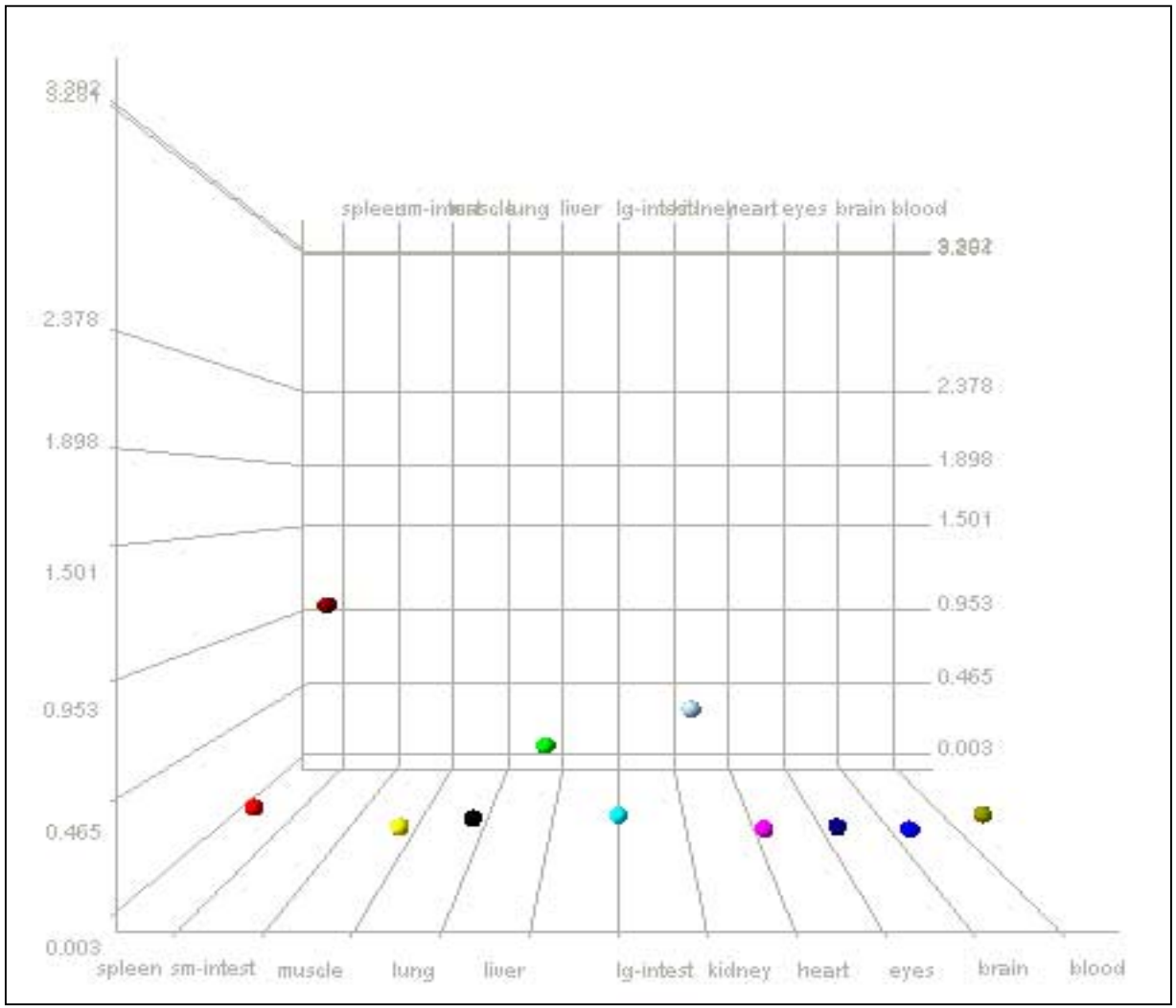
Metabolon Process Overview



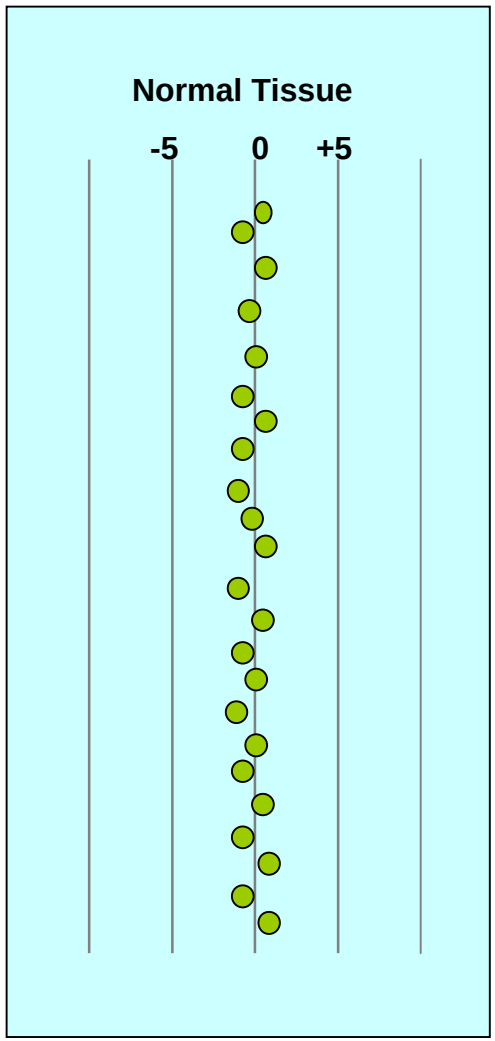
Tissue Differences



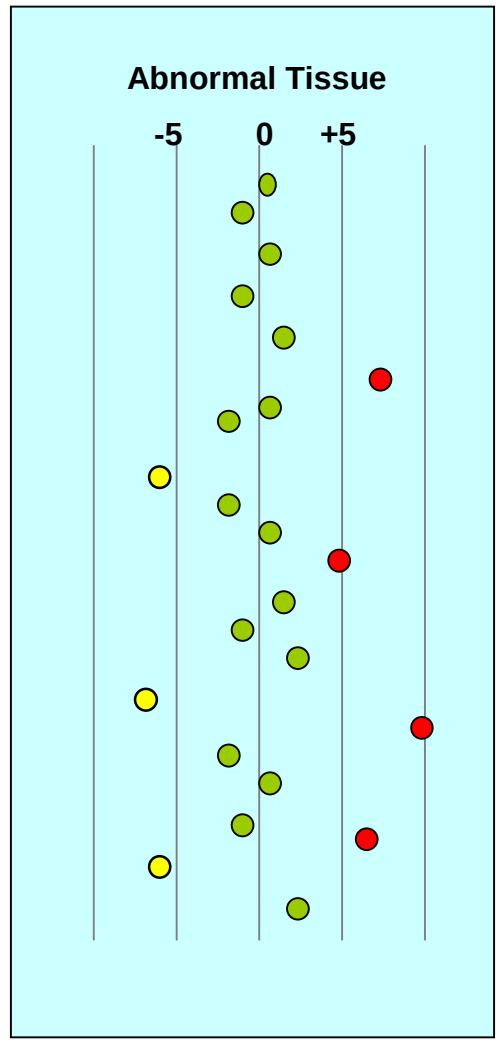
Tissue Differences



Normalized Response

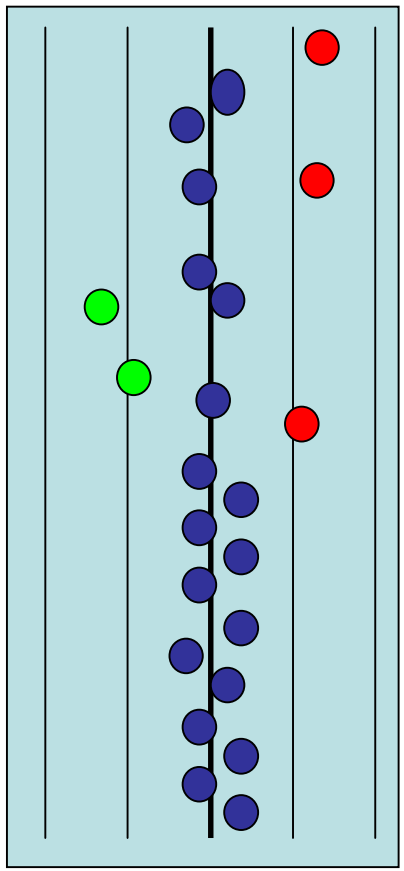


Compound 1
Compound 2
Compound 3
Compound 4
Compound 5
Compound 6
Compound 7
Compound 8
Compound 9
Compound 10
Compound 11
Compound 12
Compound 13
Compound 14
Compound 15
Compound 16
Compound 17
Compound 18
Compound 19
Compound 20
Compound 21
Compound 22
Compound 23
Compound 24

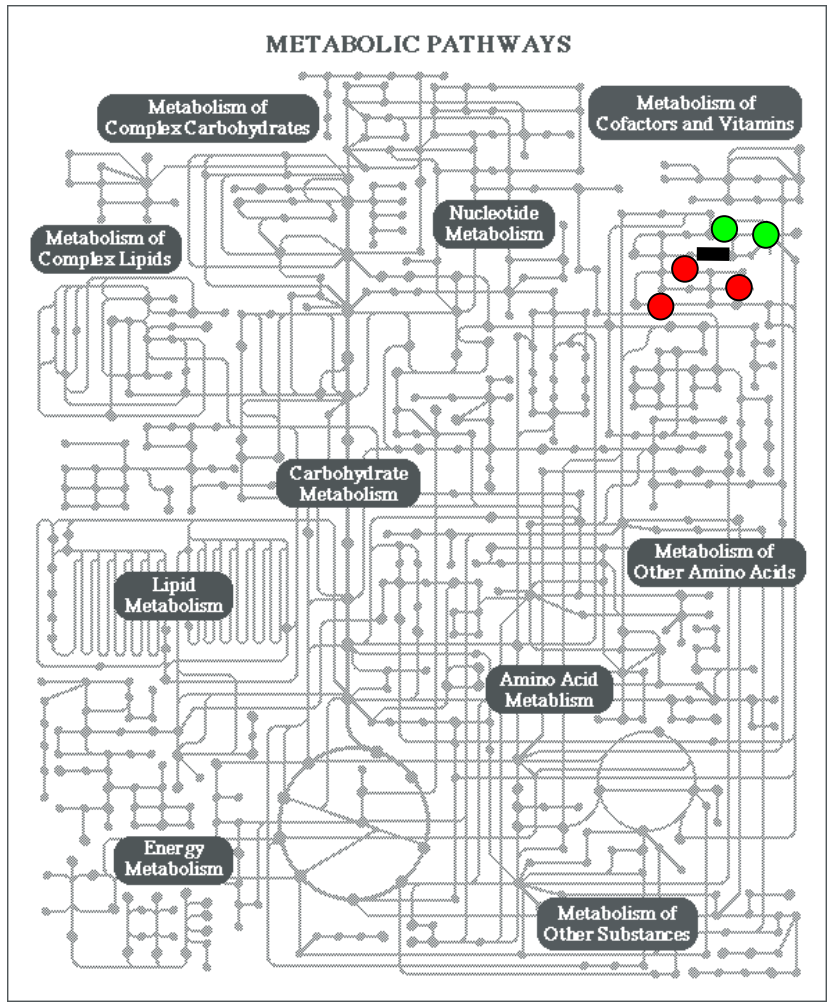


Z-term = (Obs.-Mean)/ SD

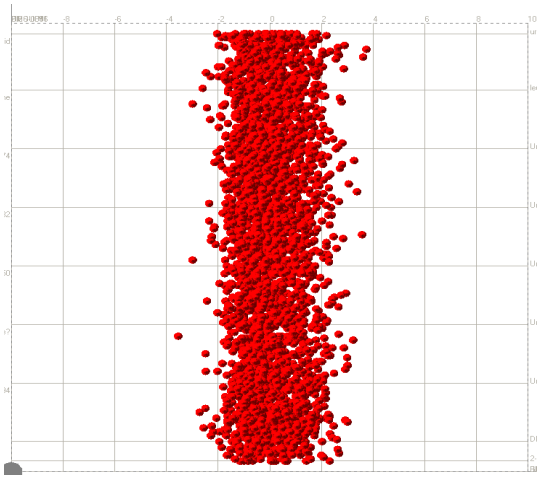
Biochemical Profile Map to Metabolic Pathways



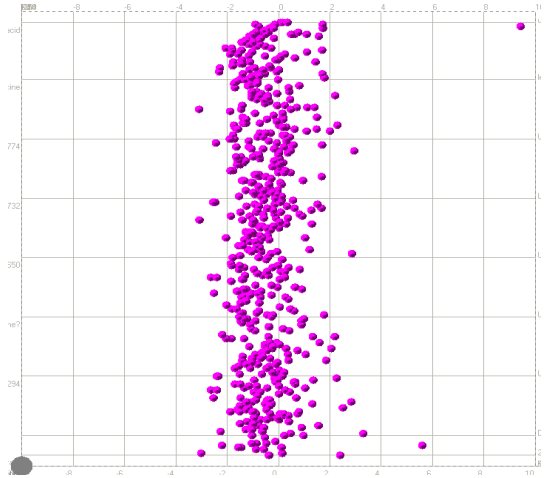
Biochemical Profile



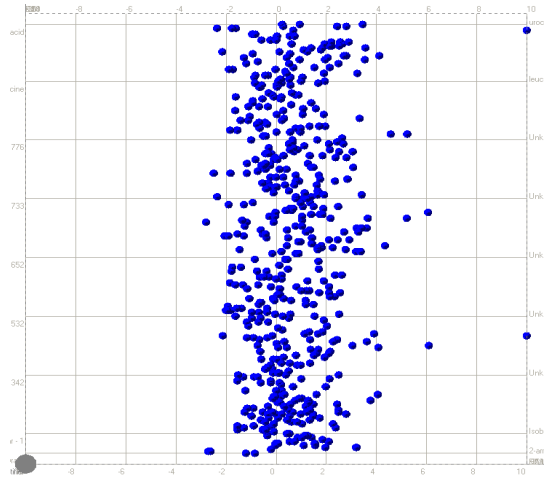
Non-Targeted Side Effects
Commercially Available HIV Drugs – *Hepatic Cell Cultures*



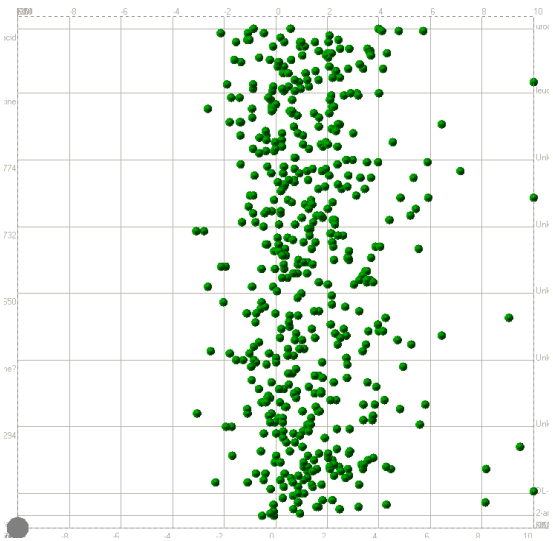
HepG2_controls



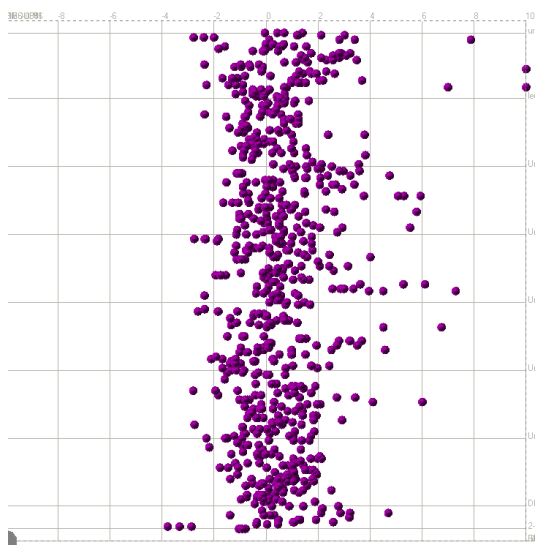
HepG2_D1



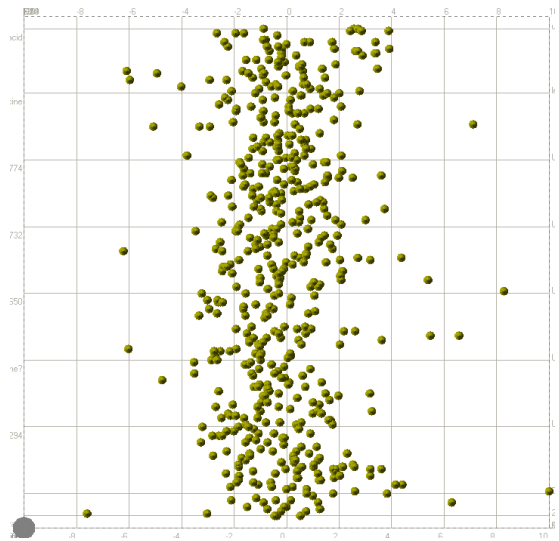
HepG2_D2



HepG2_D3



HepG2_D4



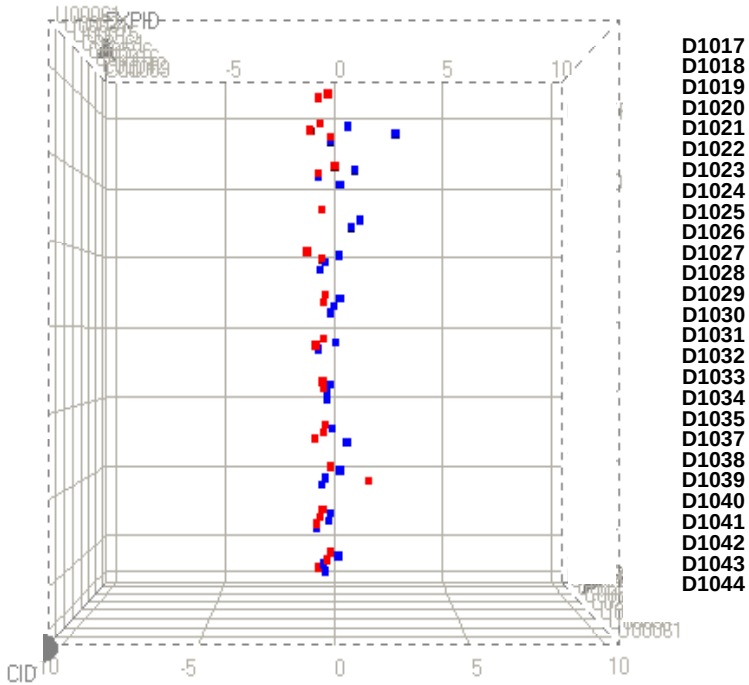
HepG2_D5

Non-Targeted Side Effects
Antibiotic Drug Leads – *Cell Cultures*

Scatter Plot

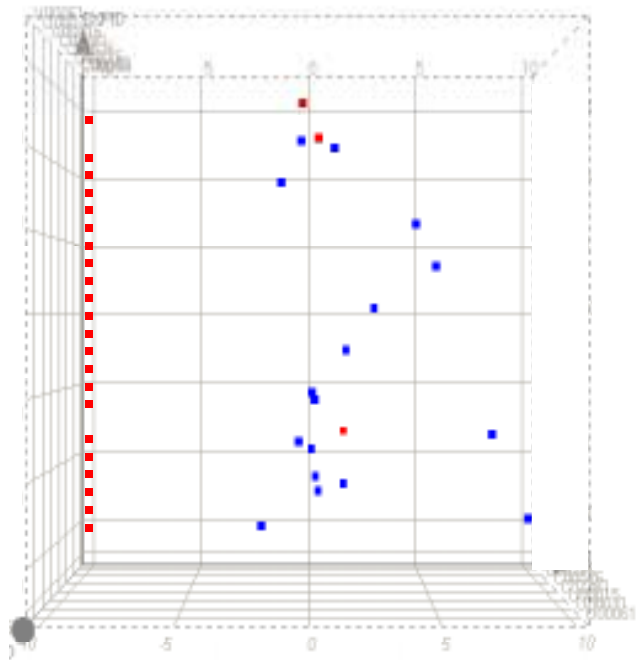
Scatter Plot

Targeted Mammalian response profile



D1017
D1018
D1019
D1020
D1021
D1022
D1023
D1024
D1025
D1026
D1027
D1028
D1029
D1030
D1031
D1032
D1033
D1034
D1035
D1037
D1038
D1039
D1040
D1041
D1042
D1043
D1044

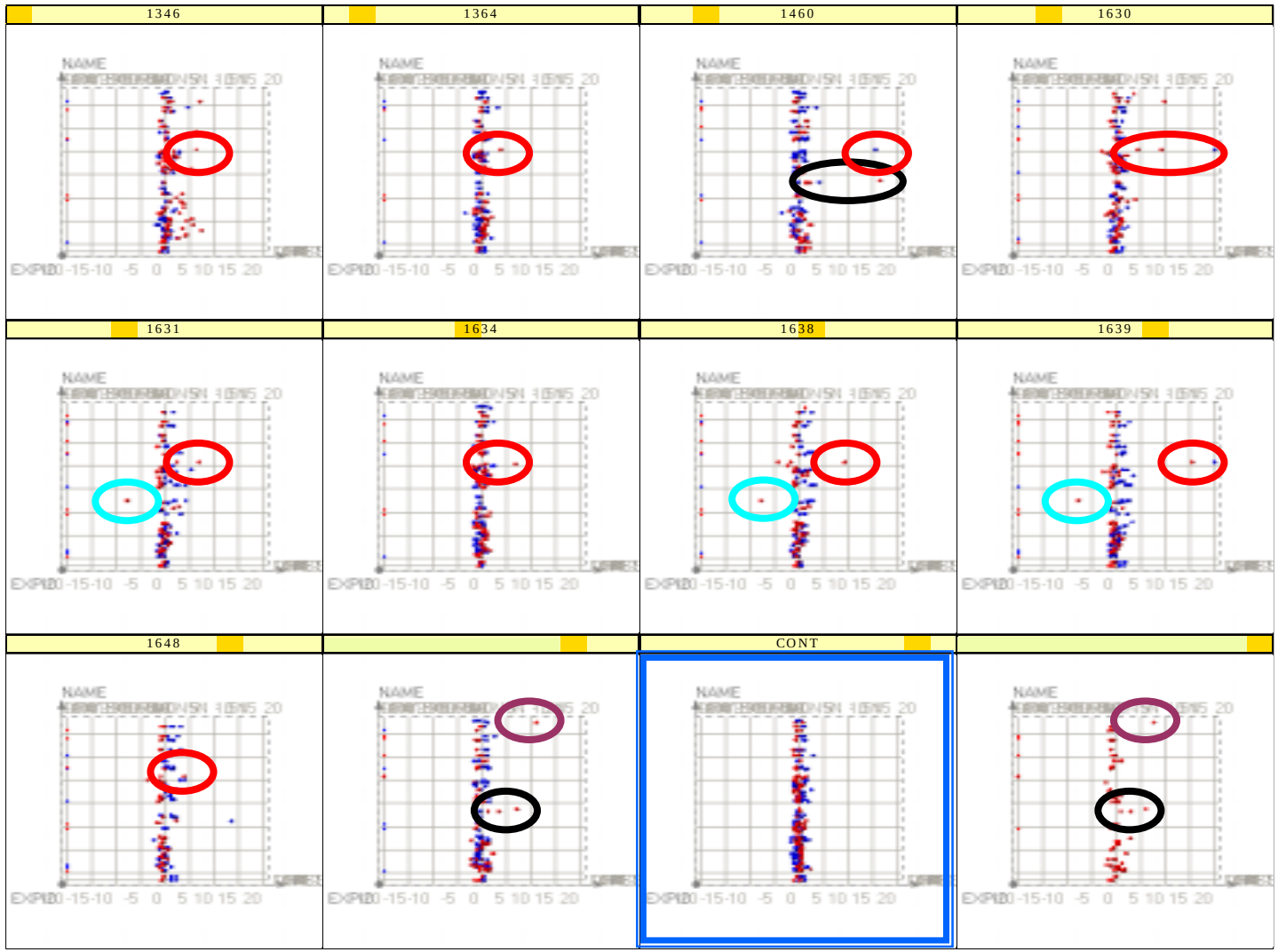
Targeted Bacterial response profile



Blue = minimal dose **Red = effective dose**

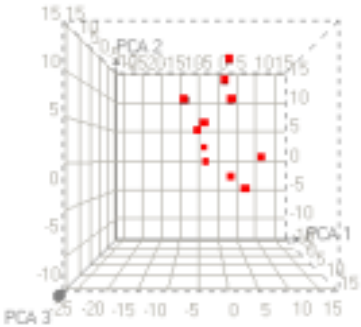
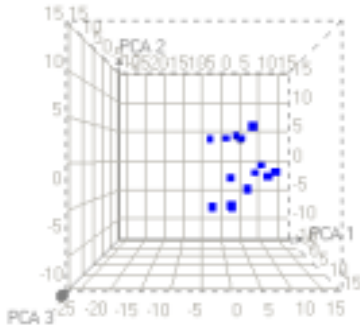
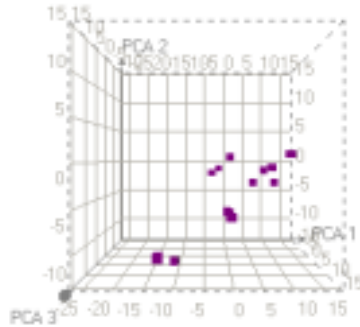
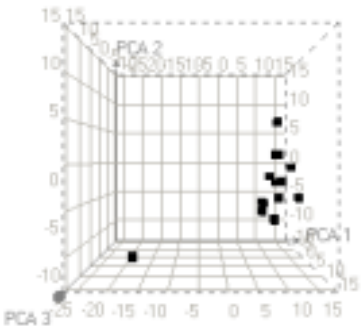
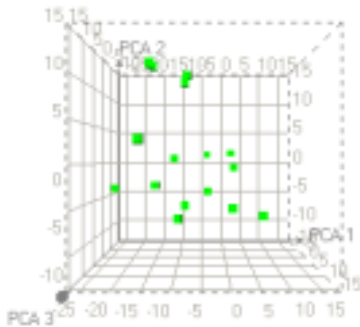
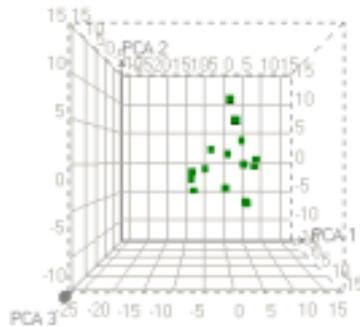
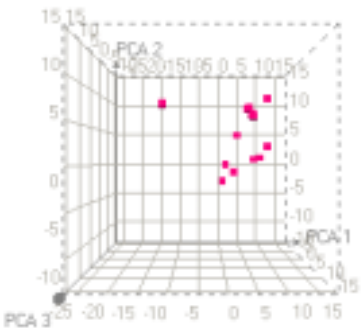
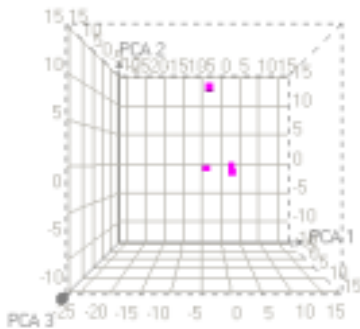
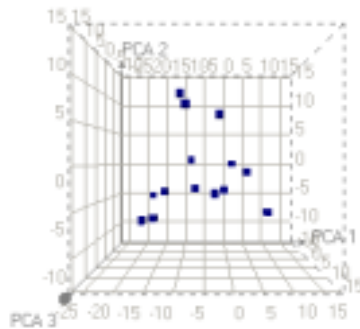
Non-Targeted Side Effects

Antibiotic Drug Leads – *Mammalian Cell Cultures*

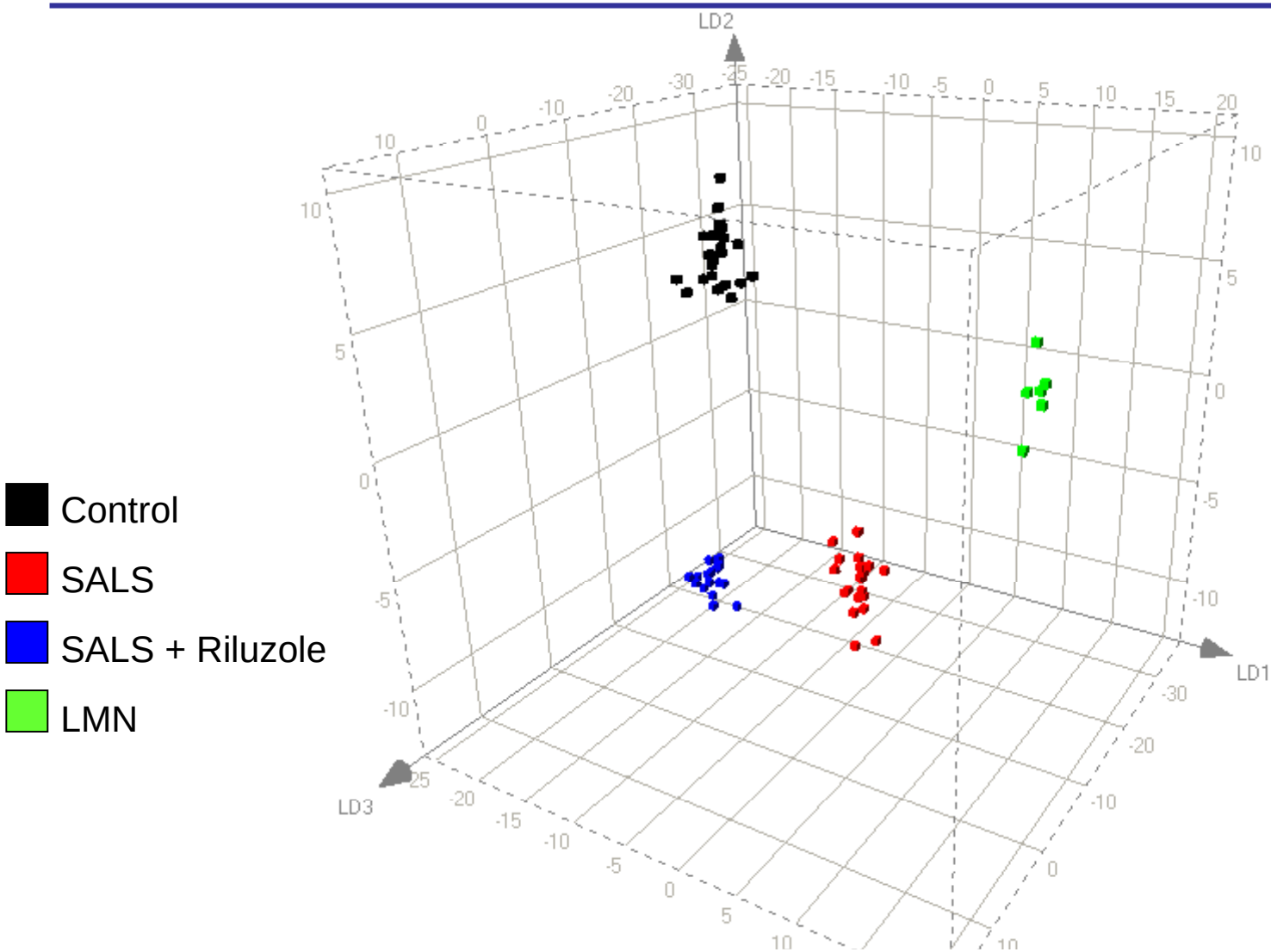


NCI 60 Cell Lines

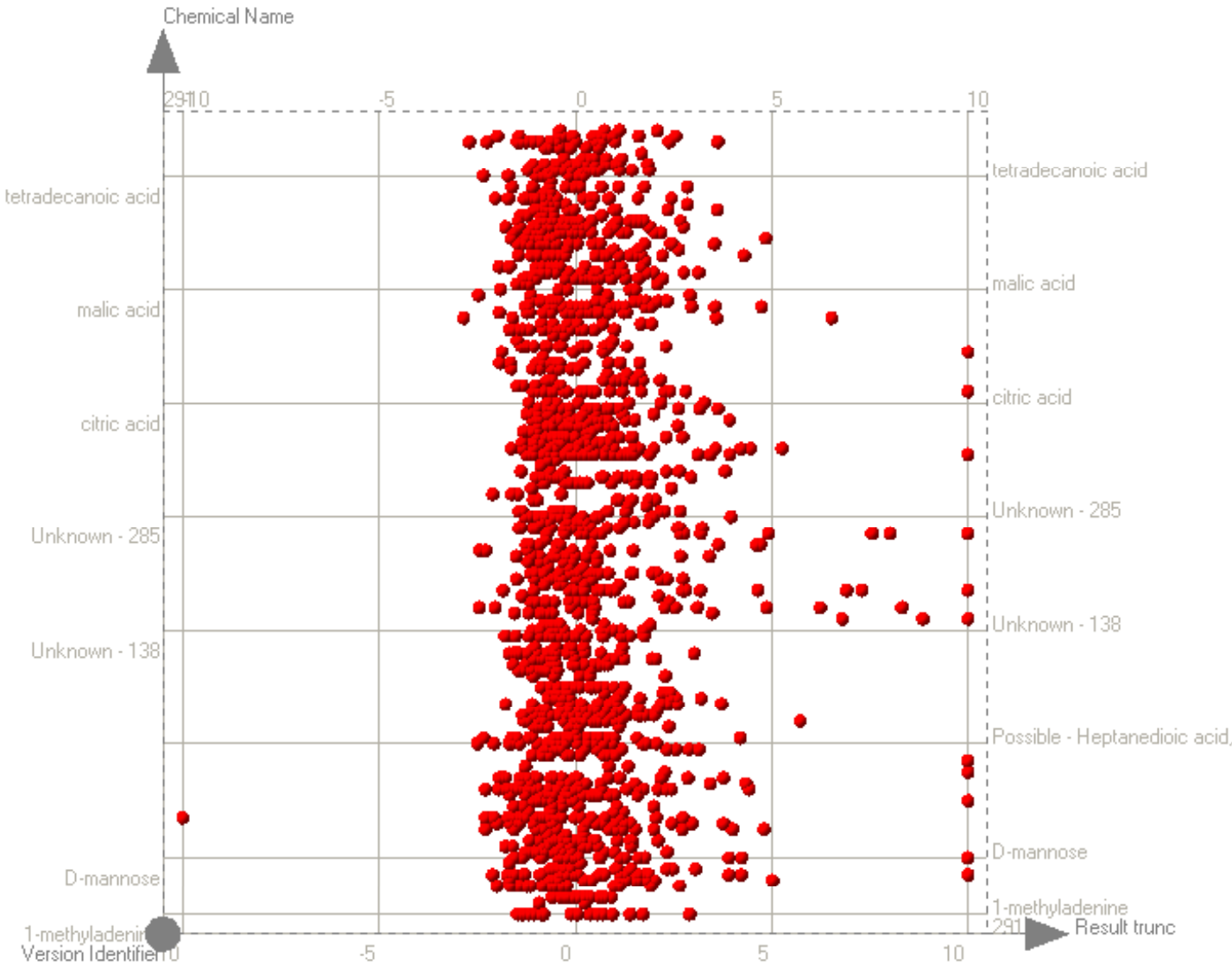
Scatter Plot

Cancer Type - CNS cancer	Cancer Type - breast cancer	Cancer Type - colon cancer
		
Cancer Type - leukemia	**Cancer Type - melanoma**	**Cancer Type - non small cell lung cancer**
		
Cancer Type - ovarian cancer	**Cancer Type - prostate cancer**	**Cancer Type - renal cancer**
		

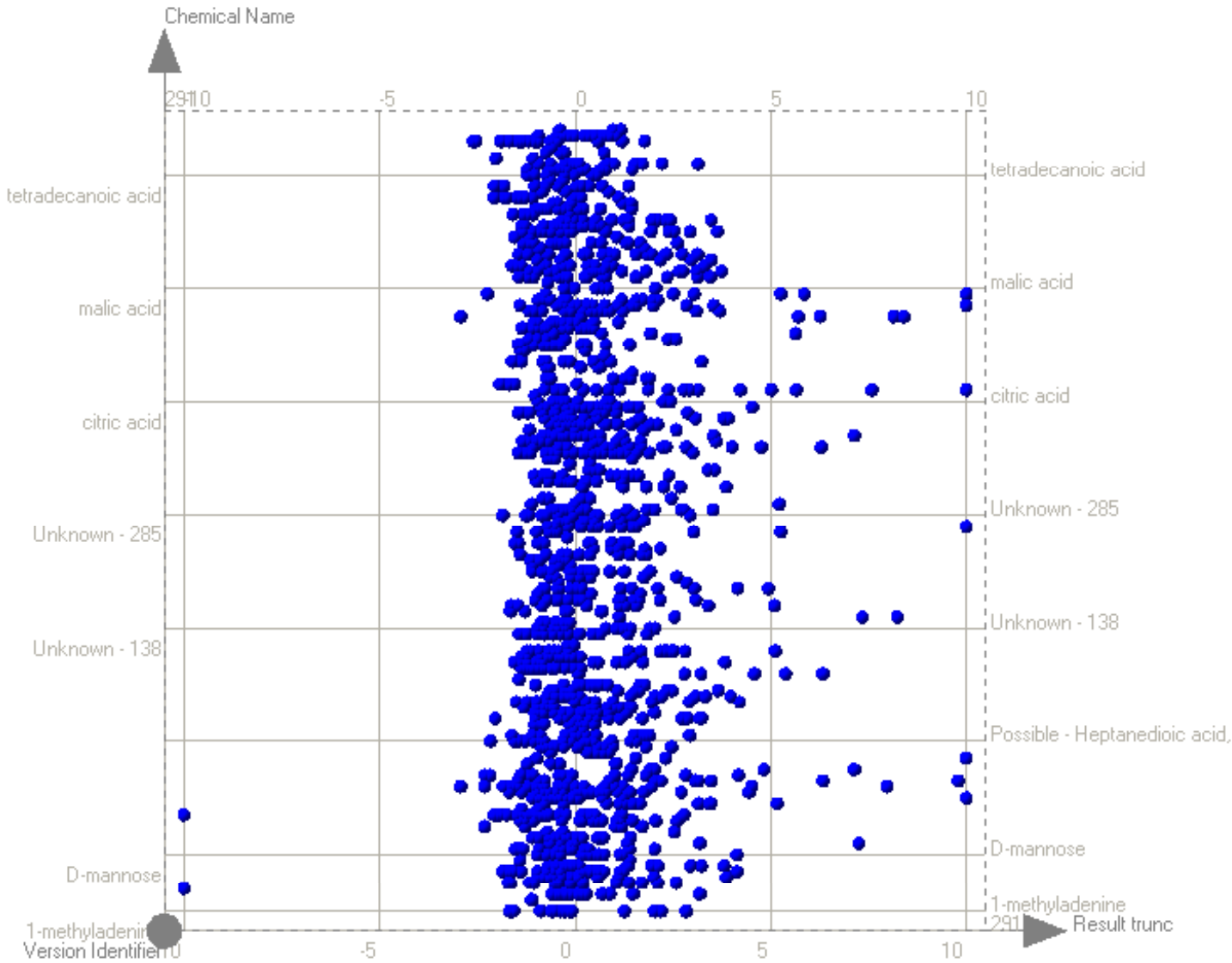
ALS Patient Stratification



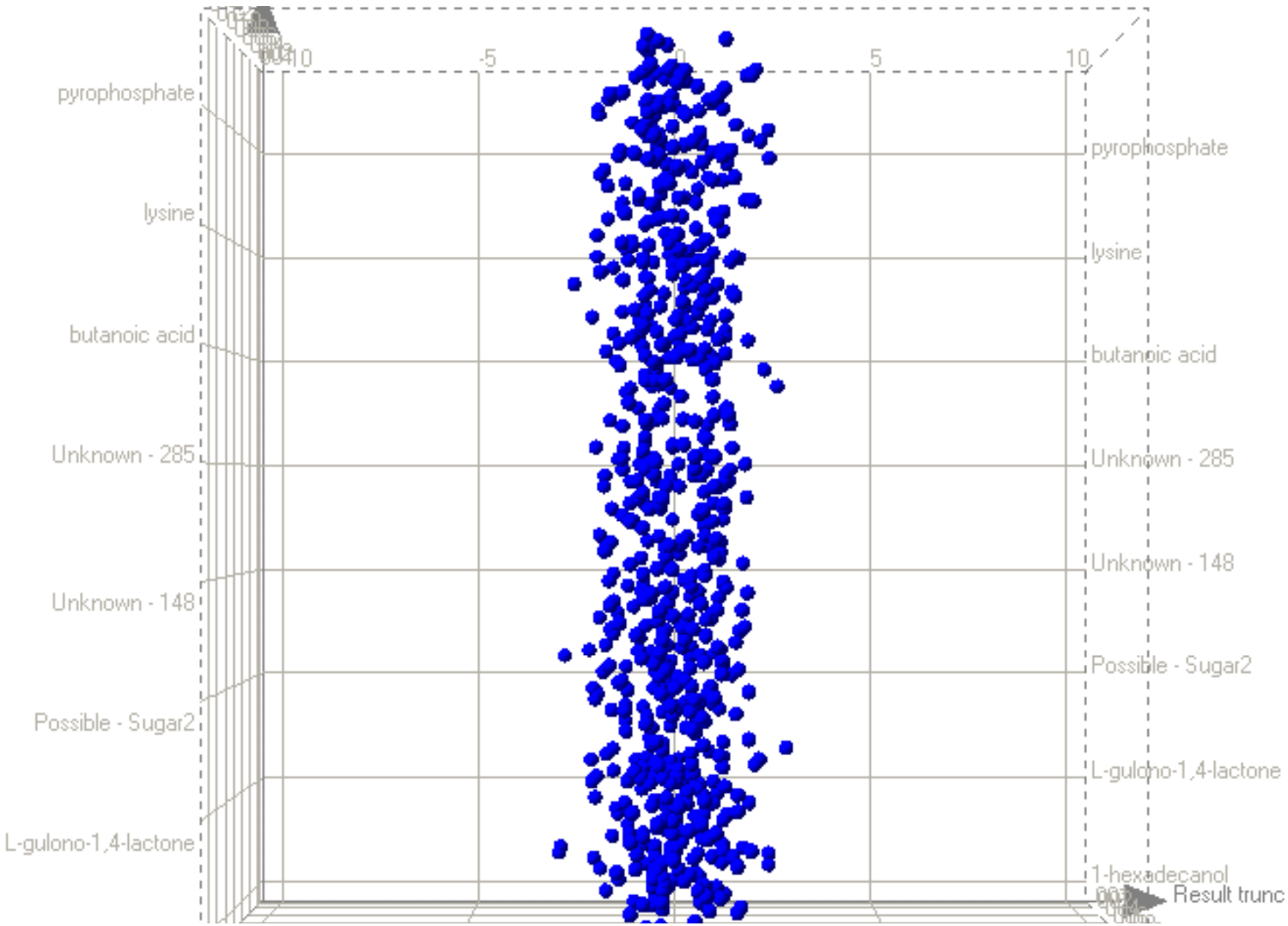
ALS Patients - Not Taking Riluzole



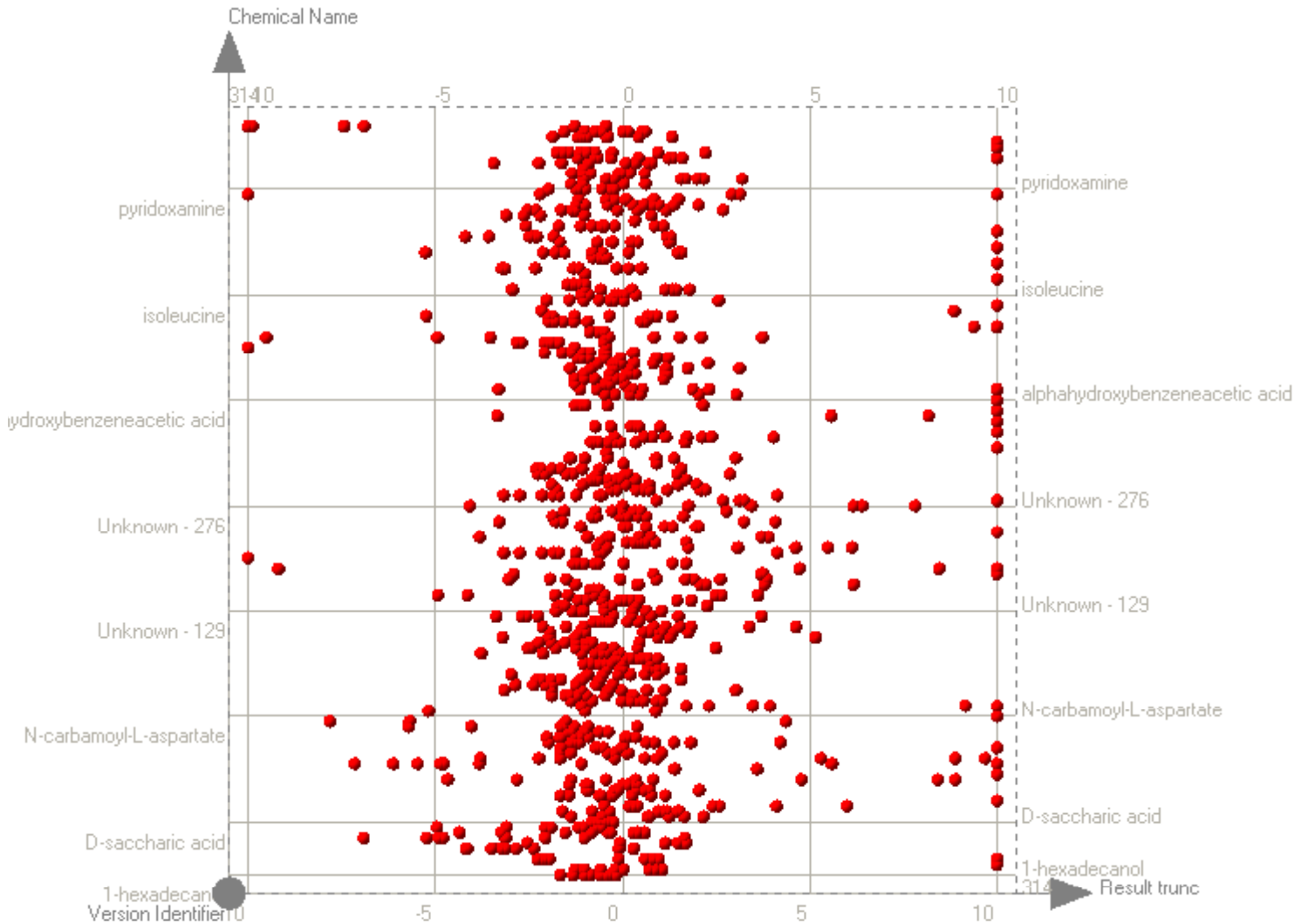
ALS Patients - Taking Riluzole



Schizophrenia - Controls



Schizophrenia - Patients



Prediction of the Clinical Class According to the Amniotic Fluid Metabolic Profile

True Class \ Predicted Class	Term Delivery	Preterm Delivery with inflammation	Preterm Delivery without inflammation
Term Delivery	39	1	0
Preterm Delivery with inflammation	7	32	1
Preterm Delivery without inflammation	2	2	29

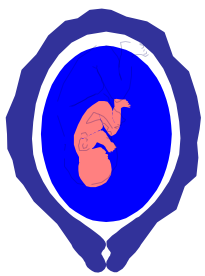
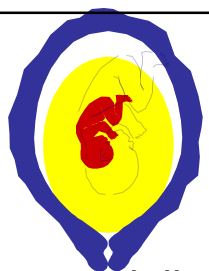
March of Dimes Saving babies, together

Random Forest Accuracy (100/113) = 88.49%

Diagnostic Indices of Amniotic Fluid Metabolome in the prediction of Clinical Class (Second Study)

	Sensitivity	Specificity
Term Delivery	98% (39/40)	88% (64/73)
Preterm Delivery with inflammation	80% (32/40)	96% (70/73)
Preterm Delivery without inflammation	88% (29/33)	99% (80/81)

March of Dimes
Saving babies, together

	Carbohydrates	Amino Acids
 Term delivery	↑	↓
 Preterm delivery	↓	↓
 Preterm delivery	↓ ↓	↑

Conclusions

- **Metabolomic analyses were used:**
  - **to find biomarkers in support of drug development, safety and efficacy.**
  - **to explore in vitro systems for differential responses to various stressors.**
  - **to examine clinical samples for diagnostic biomarkers of disease status or drug response.**


Metabolon