

# METABOLÓMICA

Coral Barbas

Danuta Dudzik

M<sup>a</sup> Fernanda Rey-Stolle

Francisco J. Rupérez

Antonia García



# ÍNDICE

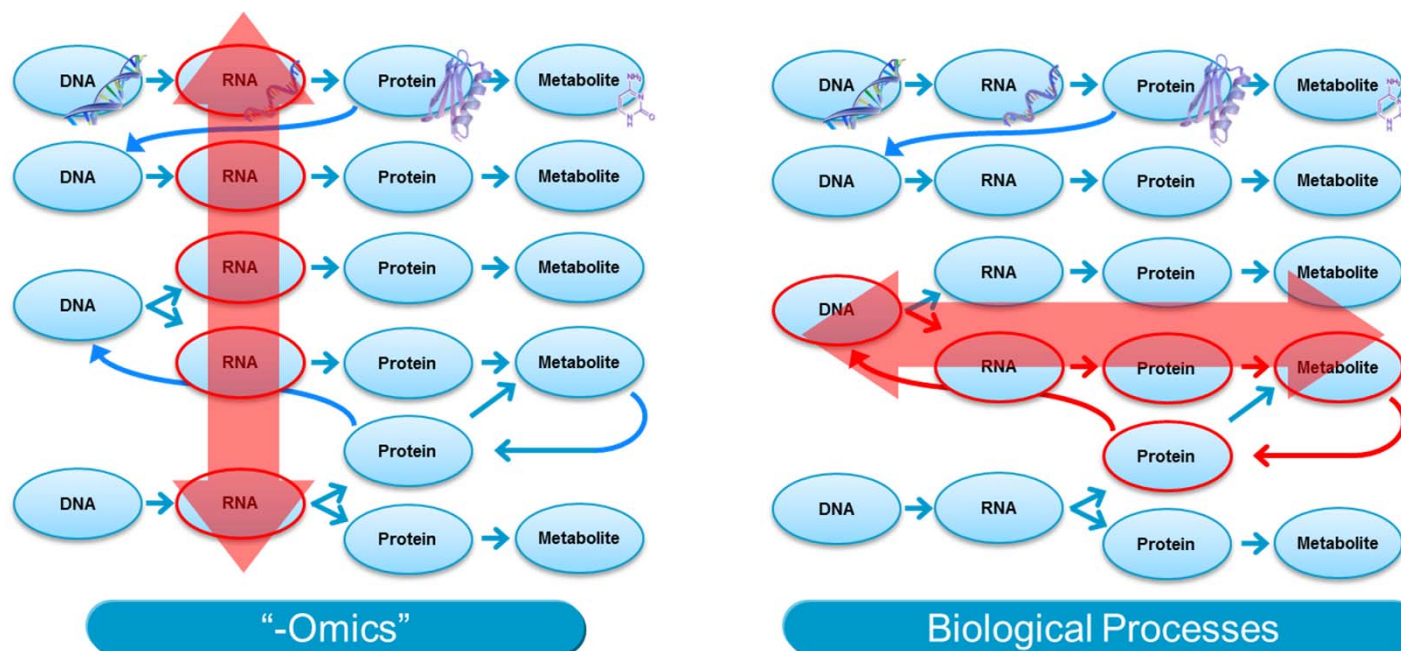
1. Introducción a la metabolómica.
2. Enfoques analíticos en la metabolómica.
  - Flujo de trabajo del estudio metabolómico
  - Procedimiento de Control de Calidad y Garantía de Calidad en la metabolómica
3. Procesamiento de datos e identificación de metabolitos
  - Flujo del procesamiento de datos
  - Tratamiento de datos en la metabolómica no dirigida
  - Identificación de metabolitos
  - Análisis estadístico
4. Análisis de datos
  - De la identificación de datos a las rutas metabolómicas
  - Validación de biomarcadores
5. Sesiones prácticas
  - Metabolómica dirigida y no dirigida
  - Metabolómica con herramientas gratuitas en línea



# Metabolómica

La investigación «ómica», nuevo campo emergente (que incluye la genómica, proteómica y metabolómica), se ocupa de la caracterización **completa** de los pequeños **metabolitos** moleculares presentes en sistemas biológicos.

## Ómica y Biología de Sistemas



## Anexo: Definición de Metabonómica

- Medida de la respuesta metabólica dinámica y multiparamétrica de un sistema vivo a estímulos patofisiológicos o modificaciones genéticas (Nicholson, 1999)
  - medida cuantitativa de la respuesta metabólica «total» en relación con el tiempo a estímulos patofisiológicos (nutricionales, xenobióticos, quirúrgicos o tóxicos)
- MetaboLómica - el cuadro / MetaboNómica - la película
- Hoy en día, todo es Metabolómica



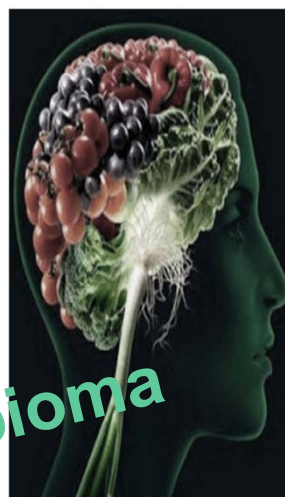
# Definición de Metaboloma

- «... el conjunto completo de metabolitos/sustancias intermedias con bajo peso molecular, que dependen de un contexto y que varían en función de la fisiología, el estado de desarrollo o patológico de la célula, tejido, órgano u organismo...» (Oliver 2002)
- **Origen:** Endometaboloma, Microbioma, Xenobioma, Nutribioma...
- **Naturaleza:** Glicoma, lipidoma, esfingolipidoma, peptidoma...
- Metaboloma ↔ Fenotipo

## Hospedador



Microbioma



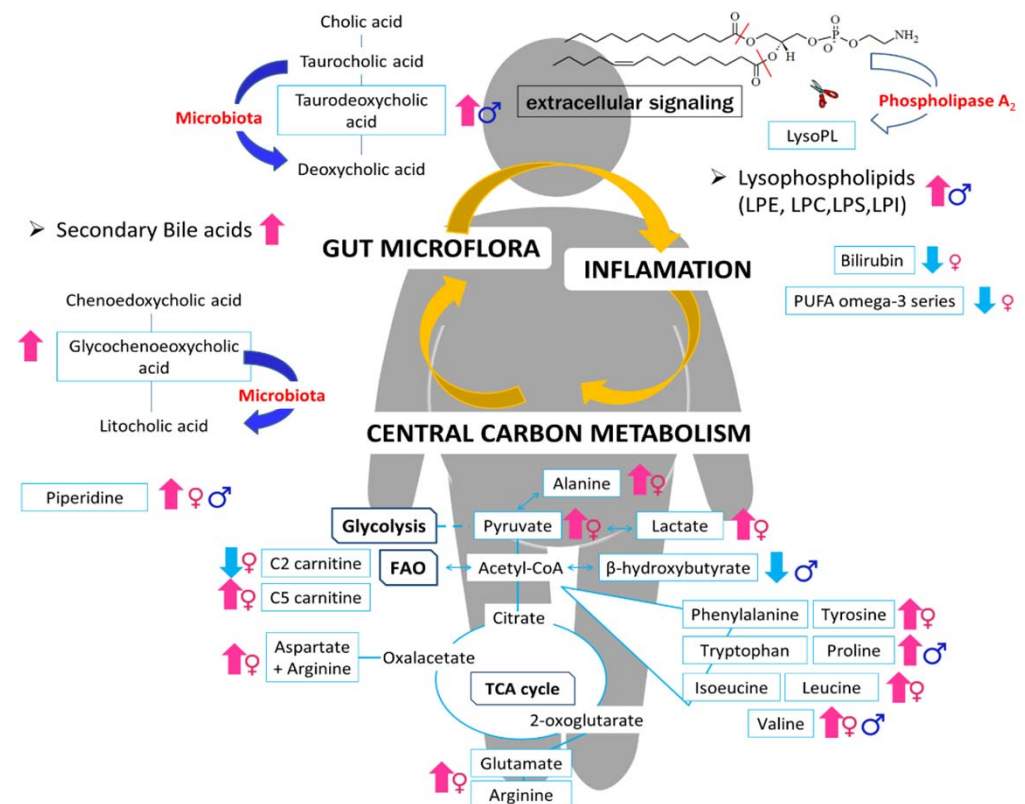
Nutribioma



Xenobioma

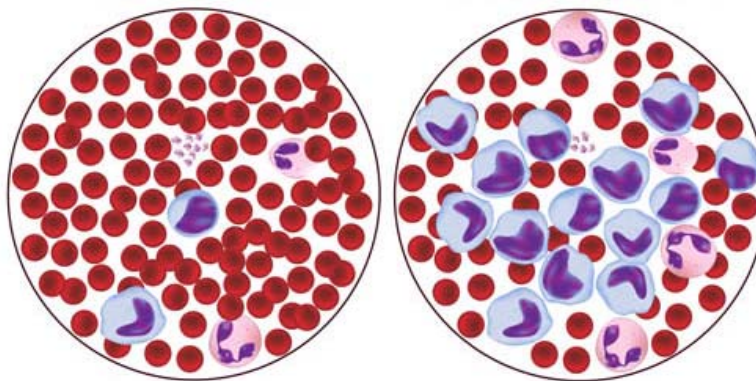
# Lo que puede aportar la metabolómica (I)

- **Perspectiva global** del estatus metabólico y de los eventos bioquímicos globales asociados a un sistema celular o biológico.
  - Situaciones patológicas sin mecanismo conocido, como la relación entre la obesidad y la resistencia a la insulina



# Lo que puede aportar la metabolómica (II)

- Identificación (propuesta) de nuevos **biomarcadores**, importantes en el proceso de descubrimiento de nuevos fármacos o como herramientas de diagnóstico in vitro.
  - Por ejemplo, nuevos biomarcadores diagnósticos para la agresividad en la leucemia linfática crónica



Utility of validated metabolites as biomarkers of aggressive state of CLL

Metabolite	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Acetylcarnitine	0.695	43.2	93.0	86.1	62.1
Butyrylcarnitine	0.548	10.8	98.0	84.4	52.4
Hexanoylcarnitine	0.690	27.0	96.0	87.1	56.8
Octanoylcarnitine	0.651	29.7	95.0	85.6	57.5
Decanoylcarnitine	0.662	27.0	94.0	81.8	56.3
Palmitoylcarnitine	0.719	40.5	94.0	87.1	61.2
Dodecanamide	0.497	8.1	100.0	100.0	52.1
Hexadecanamide	0.516	5.4	100.0	100.0	51.4
Oleamide	0.600	18.9	96.0	82.5	54.2
Linoleamide	0.672	16.2	98.0	89.0	53.9
Acylcarnitines <sup>a</sup>	0.743	32.4	95.0	86.6	58.4
FAA <sup>b</sup>	0.662	13.9	96.0	77.6	52.7
Acylcarnitines and FAA	0.750	54.0	89.0	83.1	65.9

## La metabolómica sirve para...

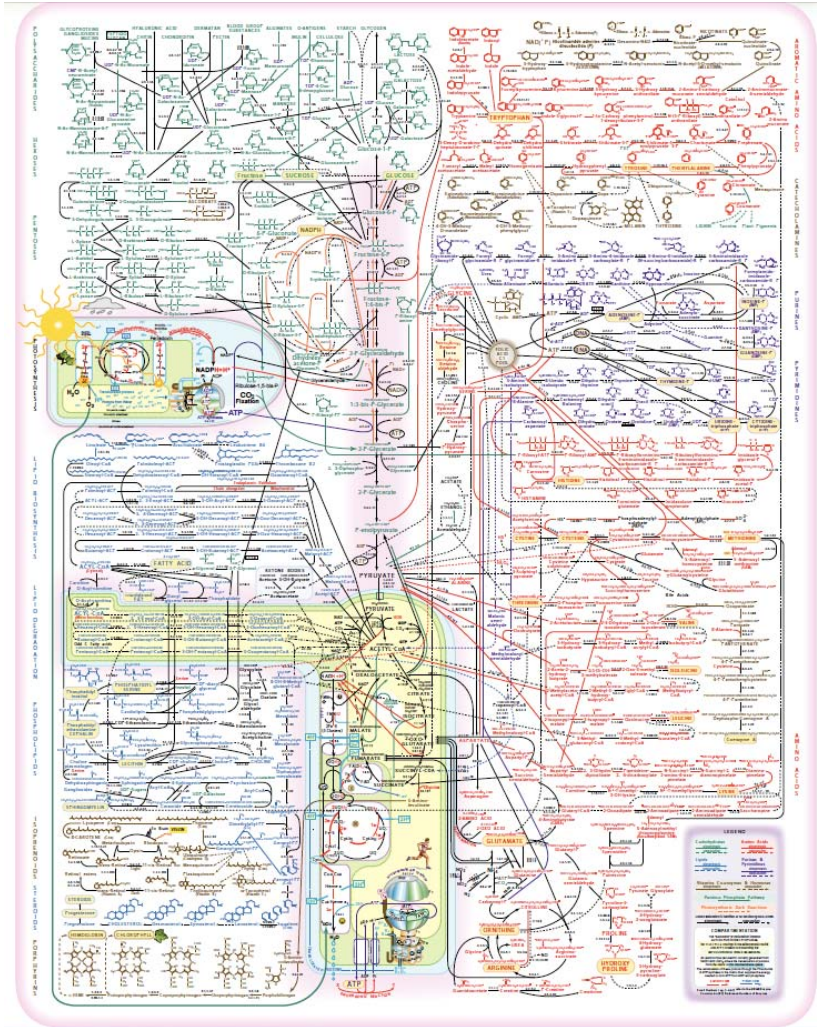
- buscar diferencias metabólicas entre grupos de muestras (caso vs. control; pre-tratamiento vs. post-tratamiento; una condición vs. otra)
- identificar compuestos que sean significativos y proponer los mecanismos
- averiguar información sobre el fenotipo
- observar los efectos de un tratamiento
- encontrar nuevos objetivos farmacológicos

## La metabolómica NO es...

- un método para revelar el destino de un metabolito o un fármaco
- un método de cuantificación
- el uso de un simple kit para cuantificar un grupo de metabolitos (se requiere NMR, MS...)
- posible sin una comparación simultánea de muestras



# Definición de Metabolismo



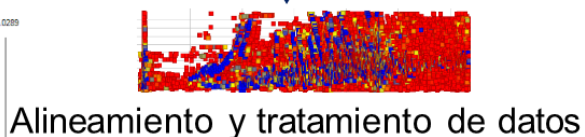
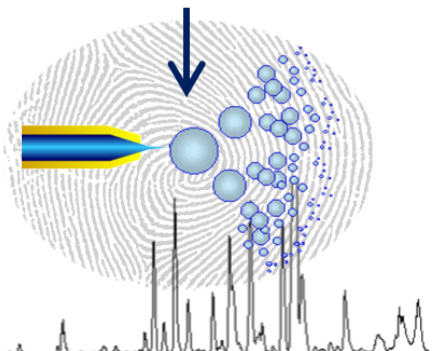
El grupo completo de procesos (bio)químicos dentro de un orgánulo, célula, tejido, órgano u organismo, esenciales para la vida

## Estrategias metabolómicas

### No dirigida

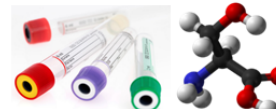


Muestras

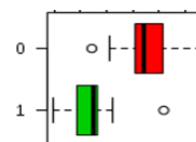
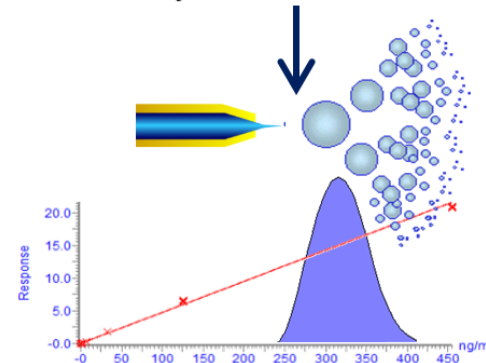


**Perfil metabólico global**

### Dirigida



Muestras y Estándares de metabolitos



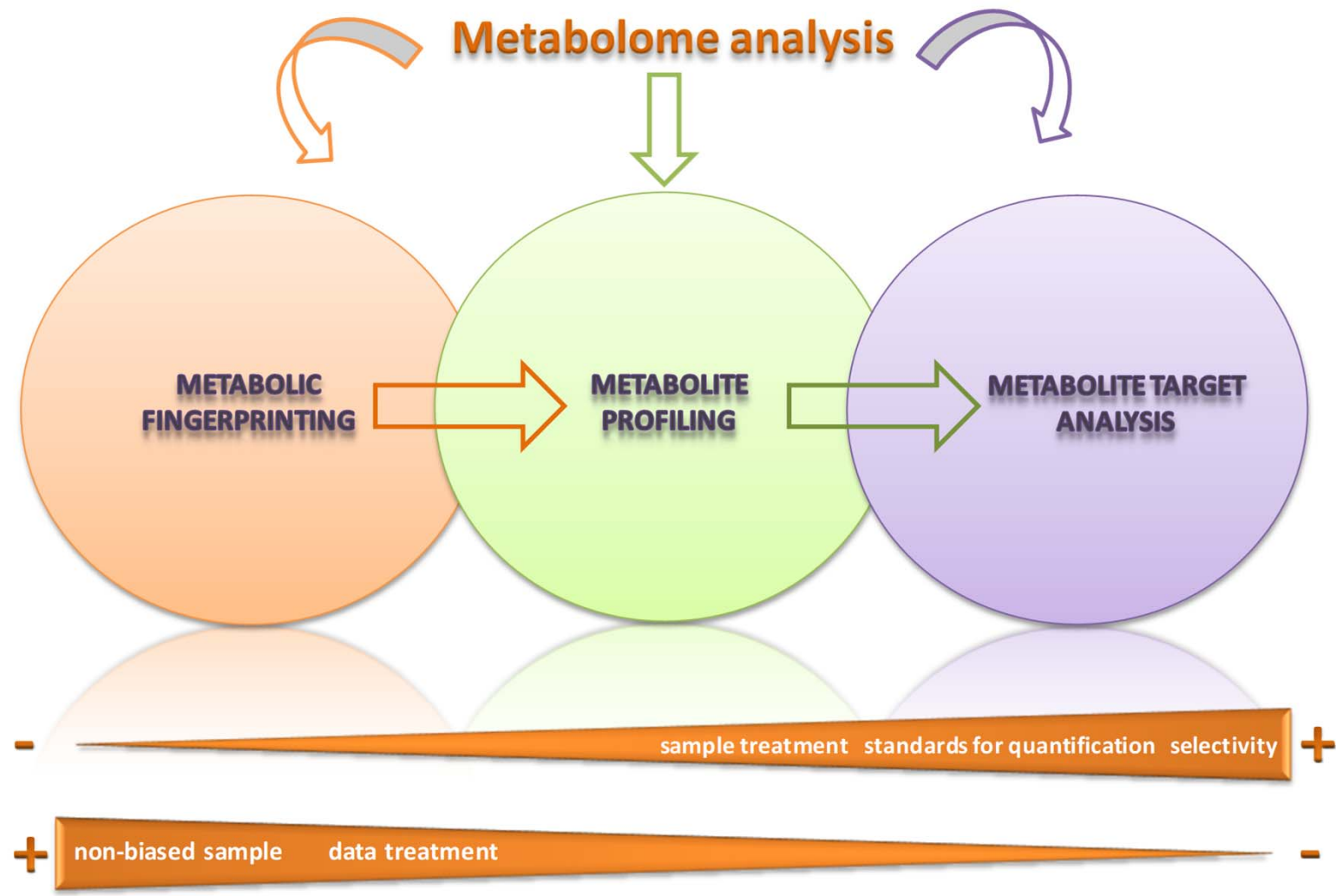
Análisis de datos/Cuantificación

Comparación de muestra y estándares

**Cuantificación de metabolitos específicos**



# Tres maneras de hacer metabolómica



# FLUJO DE TRABAJO EN METABOLÓMICA



# TÉCNICAS ANALÍTICAS

- GC/MS: Compuestos polares pequeños
  - Principalmente solubles en agua (algunos hidrofóbicos)
  - Tratamiento de muestras: Derivatización
  - Fragmentación reproducible - bases de datos
- NMR
  - Soluble en agua
  - Prácticamente sin tratamiento de muestra
  - LOD alto
- LC/MS
  - metabolitos de tamaño pequeño a grande (<1500 Da), y de polaridad media a nula
- CE/MS: Compuestos polares pequeños-medianos
  - Aminoácidos, acilcarnitinas, poliaminas, etc.
  - Sin derivatización



# Plataformas analíticas basadas en la MS en la metabolómica

## Técnica Analítica

## Aplicación

## Ventajas

## Desventajas

GC-MS

Separación, identificación, y cuantificación de metabolitos poco polares, volátiles y térmicamente estables

Elevada resolución, posibilidad de librerías de metabolitos de amplio espectro para identificación.

Imposibilidad de analizar metabolitos termoestables. Se requiere la derivatización de metabolitos no volátiles de elevado peso molecular

LC-MS

Separación, identificación, y cuantificación de numerosos grupos de metabolitos, dependiendo del tipo de columna y fase móvil

Alta sensibilidad, alta capacidad de carga de muestra, no necesaria derivatización, posibilidad de analizar compuestos termolábiles.

Disponibilidad limitada de librerías comerciales, restricción de eluyentes en LC, efecto matriz, limitado potencial de identificación a menos que se utilice como detección MS-MS

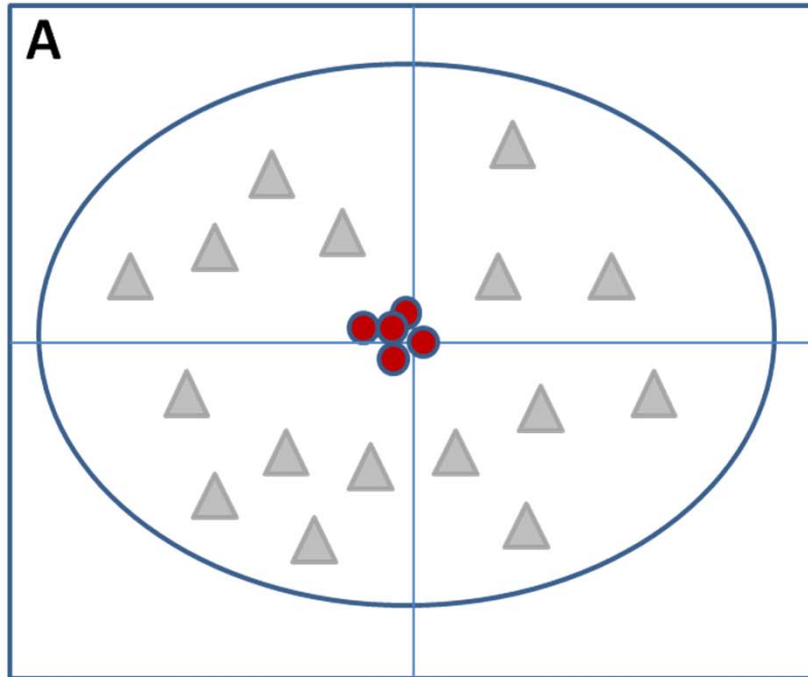
CE-MS

Separación, identificación, y cuantificación de metabolitos polares e ionizados, volúmenes de muestra muy pequeño.

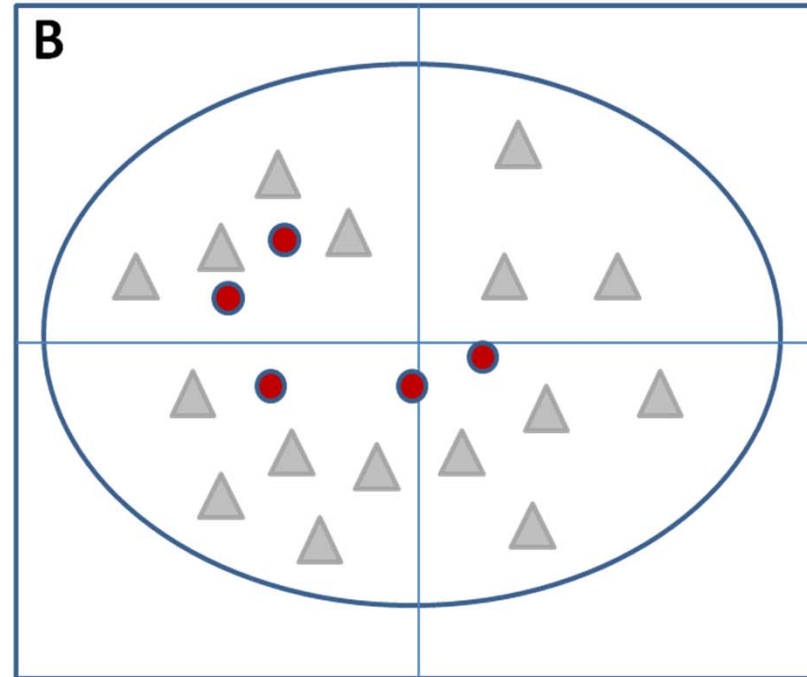
Elevada resolución y análisis rápido, útil para muestras biológicas complejas, incluso con muy poco volumen

Disponibilidad limitada de librerías comerciales. Incompatibilidad de BGE, límites de detección. Limitado potencial de identificación a menos que se utilice como detección MS-MS

# Procedimiento de Control de Calidad y Garantía de Calidad en la metabolómica



A: QC (puntos rojos) agrupadas

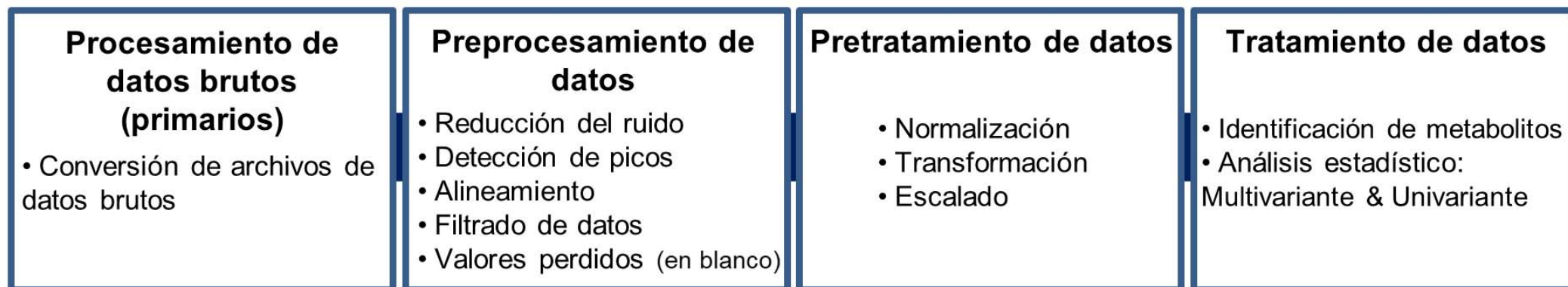


B: QC dispersas



# TRATAMIENTO DE DATOS EN METABOLÓMICA:

## Procesamiento de señales



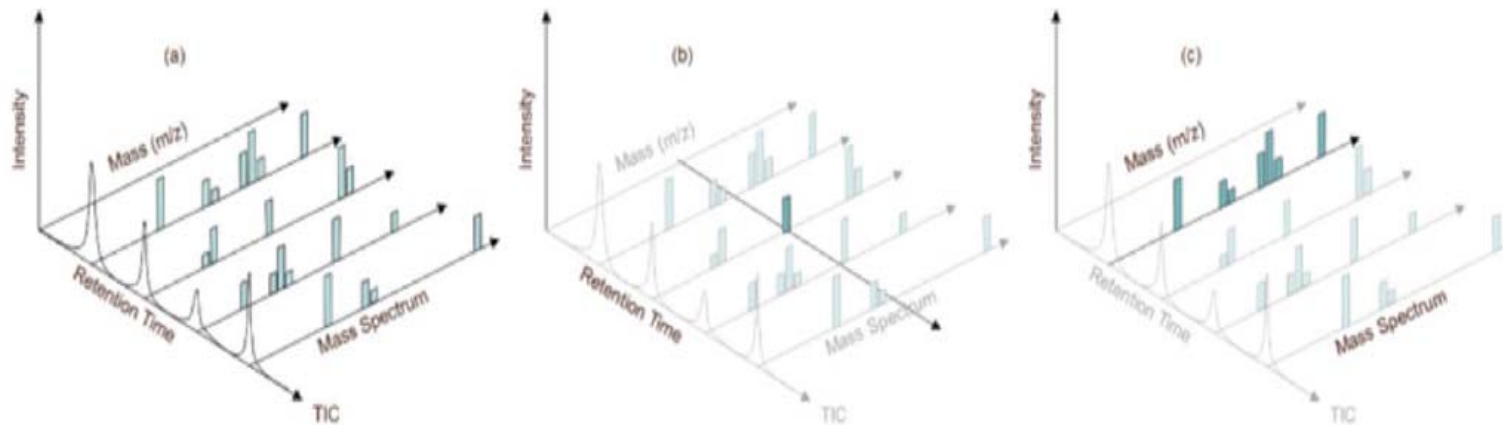
**FLUJO DEL PROCESAMIENTO DE DATOS**





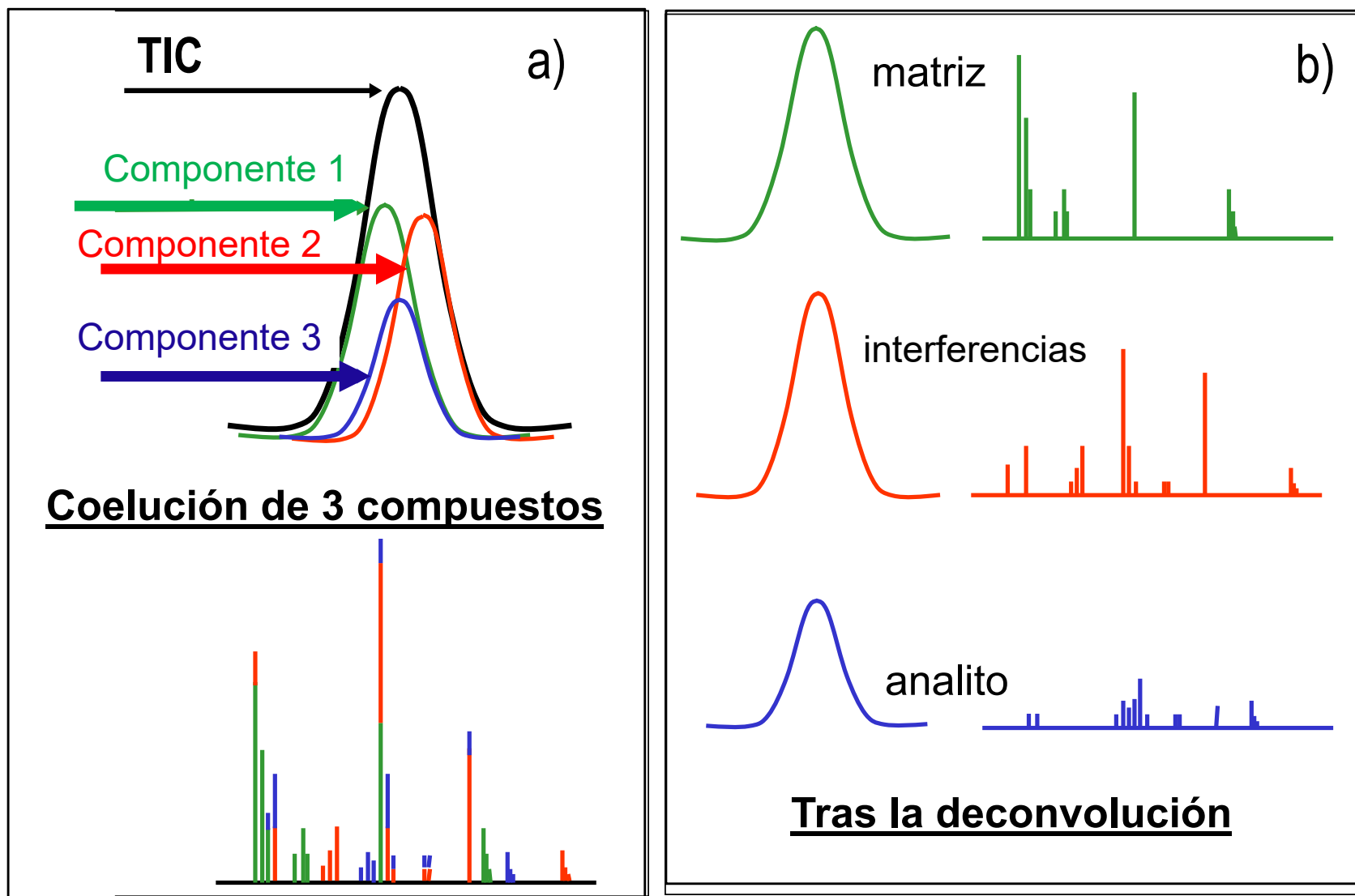
# TÉCNICA ANALÍTICA: GC-MS

- Cromatografía de gases acoplada a la espectrometría de masas
- Criterio de referencia
  - Altamente sensible y reproducible
  - Información: Calidad y Cantidad
  - Librerías de espectros para propósitos de identificación
  - El 10-20% de los compuestos conocidos se pueden analizar mediante GC
    - Alta relevancia metabólica



(a) Datos 3D de GC/MS; (b) Cromatograma de ion extraído para el ion seleccionado  
(c) Un único punto de datos en el tiempo proporciona un único espectro de masas  
*extraído de Chromatography Today*

# Deconvolución



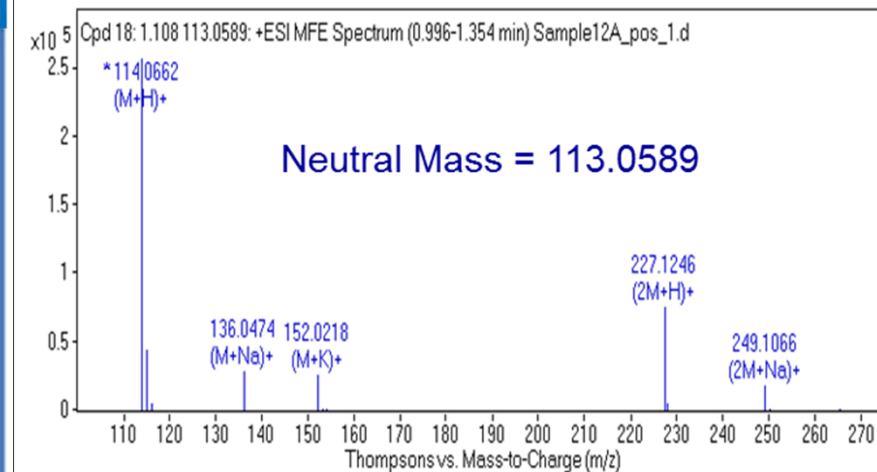
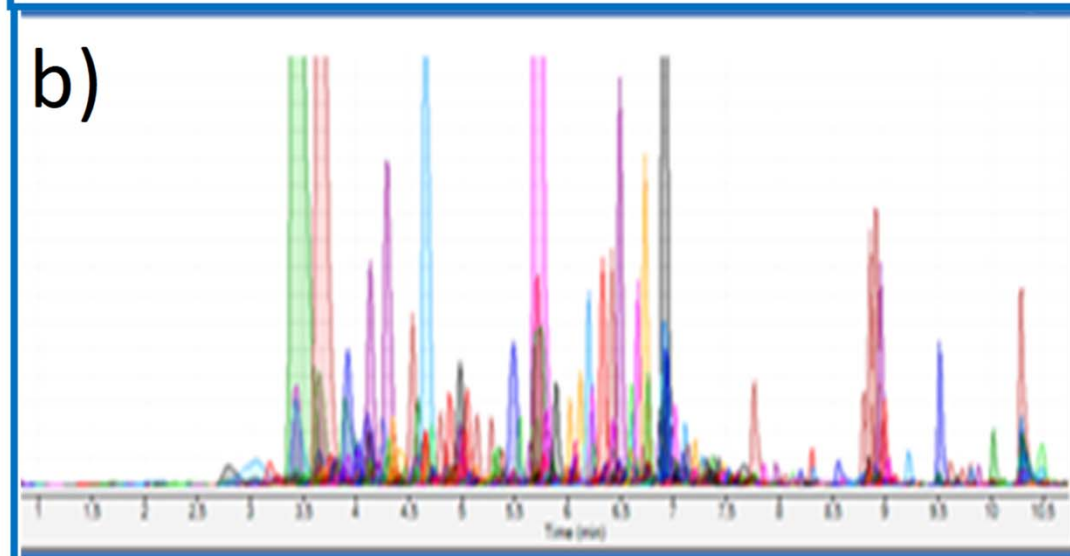
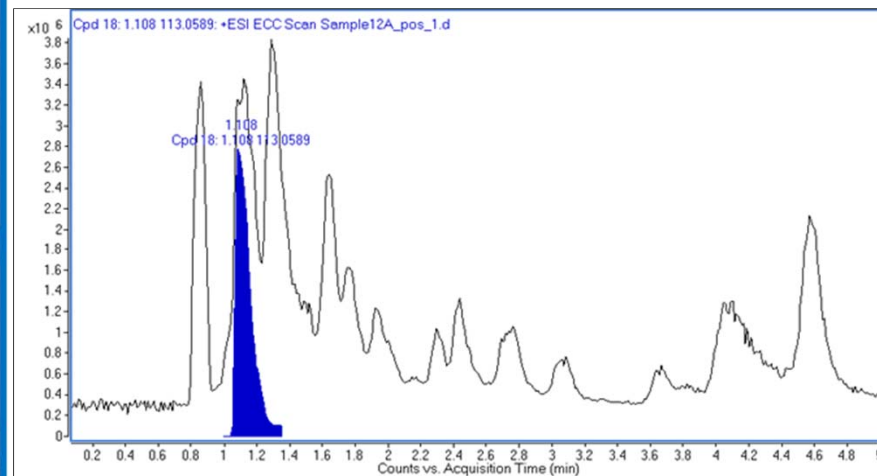
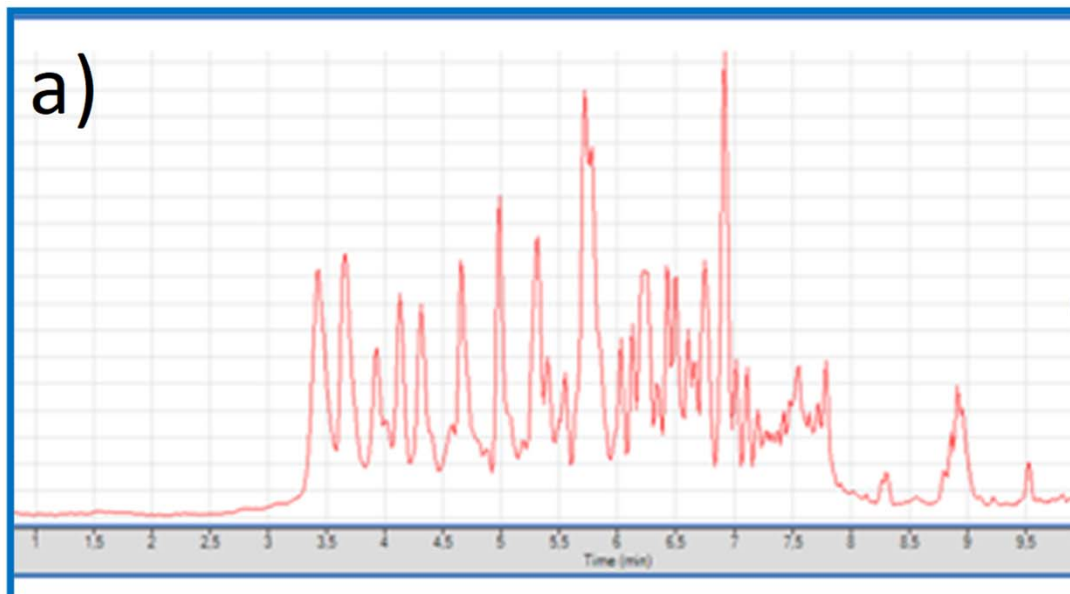
a) Antes y b) Después del proceso de deconvolución

extraído de <https://www.agilent.com/cs/library/Support/Documents/f05017.pdf>

# Deconvolución en LC-ESI-MS y CE-ESI-MS

- Métodos basados en picos
- A la hora de determinar si los distintos iones son del mismo “posible compuesto” (*feature*) el *Molecular Feature Extractor* (Agilent) considera la exactitud de las medidas de masas para iones relacionados en un grupo por su estado de carga, distribución isotópica, y las posibles relaciones químicas.
- También puede considerar iones vinculados como aductos: aductos de protón, sodio, potasio y amonio en la ionización positiva o pérdida de un protón, aductos con formiato, etc., en el modo de ionización negativa.

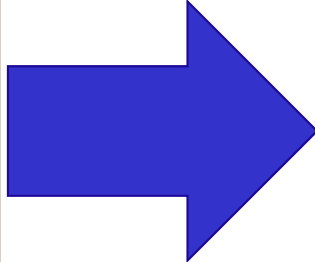
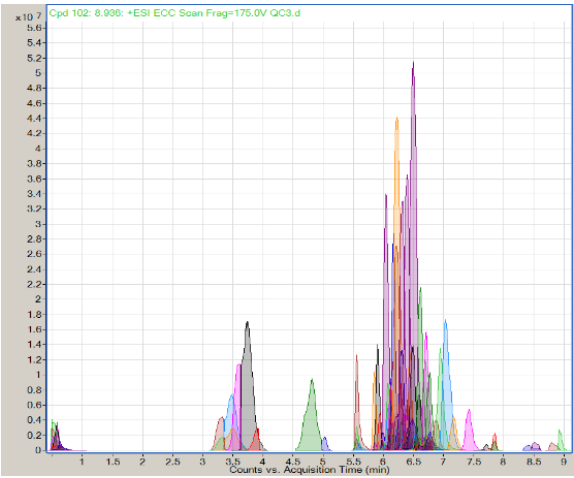
# Después de la deconvolución



a) Cromatograma de Iones Totales

b) Cromatogramas de cada uno de los compuestos obtenidos después de la deconvolución

# ¿Cromatograma o lista de características?



Automatically Show Columns

Show/Hide	Saturated	RT	m/z	Mass	Polarity	Ions	Height	Area	Vol	Quality Score
<input checked="" type="checkbox"/>	S	0.514	280.0923	279.085	Positive	5	2740215		14234373	100
<input checked="" type="checkbox"/>	S	0.517	203.0526	202.0454	Positive	6	4045612		20286412	80
<input checked="" type="checkbox"/>		0.526	140.0682	139.0609	Positive	3	1530642		7519633	100
<input checked="" type="checkbox"/>		0.529	136.0482	135.041	Positive	2	1187260		6016909	100
<input checked="" type="checkbox"/>	S	0.57	162.1126	161.1053	Positive	7	2758926		19465836	100
<input checked="" type="checkbox"/>	S	0.57	304.2998	303.2926	Positive	4	3021606		14360408	100
<input checked="" type="checkbox"/>		0.58	114.0664	113.0591	Positive	4	549599		6985240	80
<input checked="" type="checkbox"/>		0.614	175.1192	174.1119	Positive	3	760396		3860452	91.6
<input checked="" type="checkbox"/>		0.625	156.0768	155.0696	Positive	7	1055485		6005360	100
<input checked="" type="checkbox"/>		0.646	170.0927	169.0854	Positive	4	604901		3355886	100
<input checked="" type="checkbox"/>	S	3.29	520.3389	519.3316	Positive	7	3243984		36560884	80.2
<input checked="" type="checkbox"/>		3.298	544.3388	543.3315	Positive	4	1339590		12508261	87
<input checked="" type="checkbox"/>	S	3.483	520.3389	519.3316	Positive	11	5382675		86088232	85.2
<input checked="" type="checkbox"/>	S	3.5	544.3389	543.3316	Positive	7	2216628		36501788	100
<input checked="" type="checkbox"/>	S	3.573	496.3389	495.3316	Positive	6	8281163		80624664	86.1
<input checked="" type="checkbox"/>	S	3.746	496.3388	495.3316	Positive	13	11742118		200075408	80
<input checked="" type="checkbox"/>	S	3.89	522.3545	521.3472	Positive	8	2204035		17763280	87
<input checked="" type="checkbox"/>	S	4.801	524.3702	523.3629	Positive	12	6862920		111854136	100
<input checked="" type="checkbox"/>		5.027	524.3702	523.3629	Positive	6	1308318		8748089	87
<input checked="" type="checkbox"/>		5.559	163.0393	162.032	Positive	4	1349239		5379156	100
<input checked="" type="checkbox"/>	S	5.561	391.2839	390.2767	Positive	15	7367381		51796644	100
<input checked="" type="checkbox"/>	S	5.561	149.0235	148.0162	Positive	4	2915086		12886771	100
<input checked="" type="checkbox"/>		5.597	338.3418	337.3345	Positive	9	787867		4058574	100
<input checked="" type="checkbox"/>	S	5.849	675.5425	674.5353	Positive	7	6821314		39496860	100
<input checked="" type="checkbox"/>		5.857	627.5339	626.5266	Positive	3	712763		3673685	100
<input checked="" type="checkbox"/>	S	5.904	701.5583	700.551	Positive	8	8615328		59468044	100
<input checked="" type="checkbox"/>	S	5.941	689.558	688.5507	Positive	8	3178377		18867332	100
<input checked="" type="checkbox"/>		5.991	754.5372	753.5299	Positive	4	737180		4127601	100
<input checked="" type="checkbox"/>		5.995	730.5360	729.5297	Positive	7	1506513		8484420	100

Chromatogram Results | MS Spectrum

- **Alineamiento**

- Los desplazamientos de los picos se observan a través del eje del RT
- Dos grupos:
  - se alinean los datos antes de la detección de picos
  - métodos de alineamiento basados en el pico: se alinean en todas las muestras los picos espectrales detectados
  - programas:
    - MetaboAnalyst ([metaboanalyst.ca](http://metaboanalyst.ca))
    - mzmine and mzmine2 (<http://mzmine.sourceforge.net/>)
    - metAlign
    - BinBase ([fiehnlab.ucdavis.edu](http://fiehnlab.ucdavis.edu))
    - xcms and xcms2 (Scripps)
    - metaXCMS (Scripps)
    - XCMS Online (Scripps)

- **Valores en blanco**

- Problemas en nuevos análisis
- Distintas estrategias
  - Sustituir por la mitad del mínimo, por media/mediana, el k vecino-más-cercano (KNN), el PCA probabilístico (PPCA), el método PCA bayesiano (BPCA), o la Descomposición en Valores Singulares (SVD), etc.

- **Filtración**

- Variables de tamaños muy pequeños - detectados usando la media o la mediana
- Variables que son prácticamente constantes - detectadas usando la desviación estándar (SD)
- Variables que muestran baja repetibilidad - medidas usando la muestra QC



# Pretratamiento de datos

- Normalización

- Normalización **específica de muestra** (i.e. peso, volumen)
- Normalización por **suma** o **mediana**
- Normalización por **muestra** de referencia
- Normalización mediante muestra **combinada** a partir de un grupo de control
- Normalización por **característica** de referencia
- Normalización por **cuantiles**

- Transformación de datos

- Transformación **logarítmica**
- Transformación de **raíz cúbica**

- Escalado de datos

- Centrado a la **media**
- **Autoescalado** (centrado a la media y dividido por la desviación estándar de cada variable)
- **Escalado Pareto** (centrado a la media y dividido por la raíz cuadrada de la desviación estándar de cada variable)
- **Escalado por rango** (centrado a la media y dividido por el rango de cada variable)

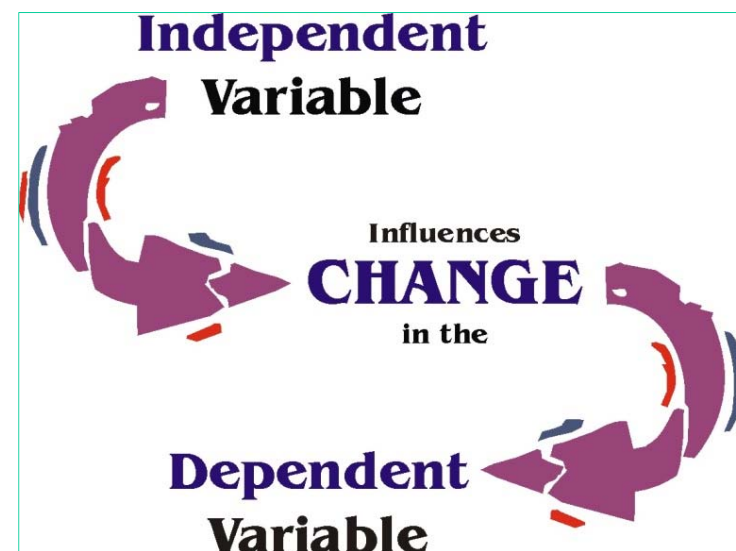
# Estadística para Metabolómica

## Objetivos:

- detectar diferencias entre grupos de muestras a nivel químico
- categorizar compuestos de acuerdo a su importancia relativa para la diferenciación de muestras

## VARIABLES

- **variable dependiente:** representa el resultado o el efecto, o se evalúa para comprobar si existe un efecto, p. ej.: abundancia de metabolito
- **variable independiente:** representa las entradas o las causas, o se evalúan para determinar si son las causas, p. ej.: condiciones de tratamiento dentro del experimento

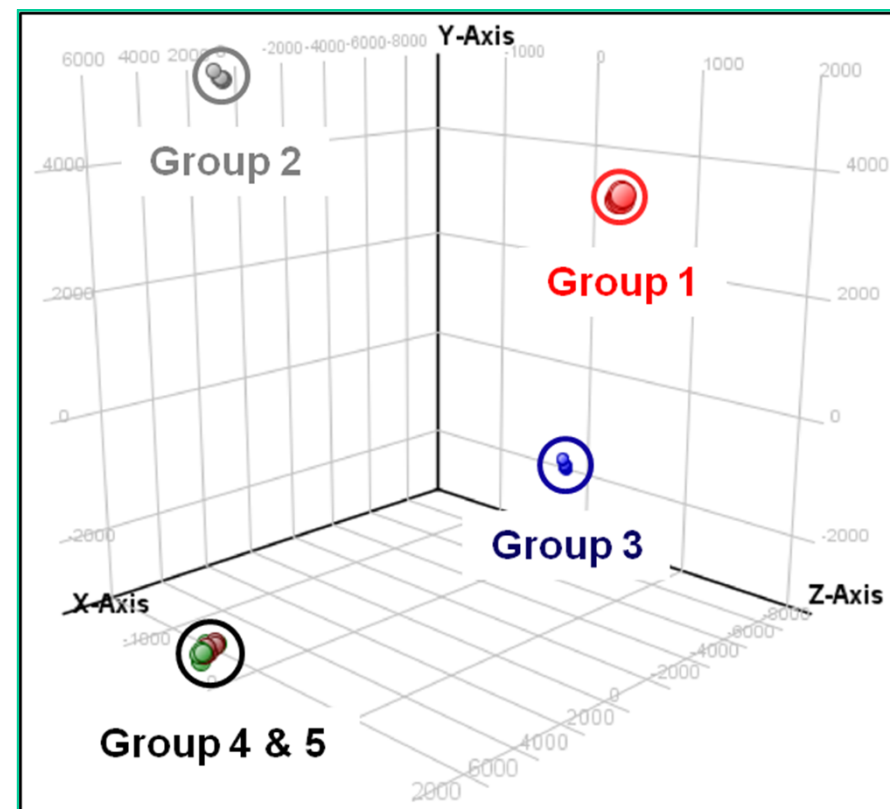


## TIPOS

- **Análisis univariante UVA:**
  - Distribución normal: Prueba *t* de Student, ANOVA
  - Distribución no normal: prueba de la U de Mann-Whitney, Kruskal-Wallis
- **Análisis multivariante MVA:** PCA, PLS-DA, OPLSDA

# PCA

- utilizado como herramienta en análisis exploratorio de datos
- cada punto representa gráficamente cada muestra medida
- el algoritmo no tiene conocimiento de las asociaciones en grupo de las muestras - análisis *no supervisado*
- el primer compuesto principal explica la mayor parte de la variación
- las cargas de compuestos indican el impacto del compuesto en el análisis
- cada punto es la suma de las cargas de compuestos de una muestra
- la densidad de la agrupación refleja la variación de las muestras



# Predicción de clases

un algoritmo que utiliza datos previos para predecir los resultados de observaciones futuras

- el algoritmo tiene conocimiento de las asociaciones en grupo de las muestras - análisis *supervisado*
- algoritmos habituales
  - **Análisis discriminante por mínimos cuadrados parciales (PLS-DA)**
  - Máquinas de soporte vectorial
  - Árbol de decisión
  - Bayesiano ingenuo
  - Red neuronal

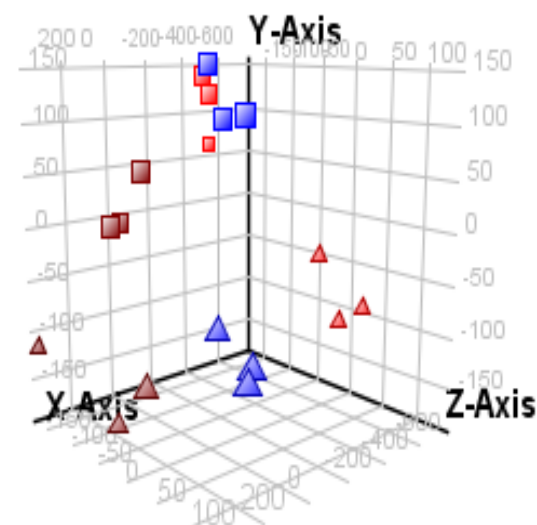
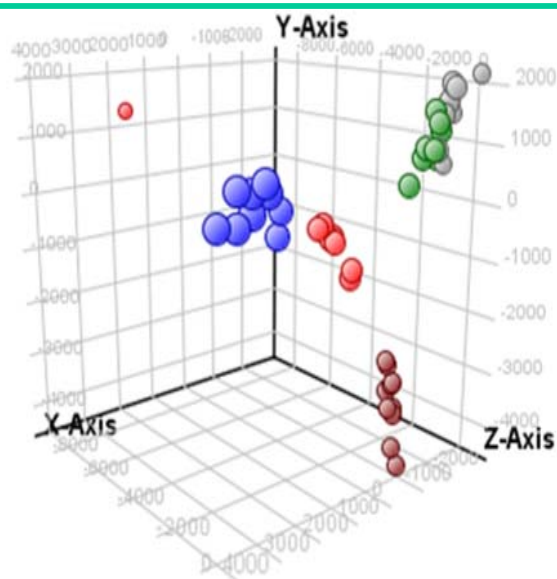


# Predicción de clases: PLS-DA

## Análisis Discriminante por Mínimos Cuadrados Parciales Análisis Discriminante por Proyección en Estructuras Latentes

un método estadístico que guarda cierta relación con el análisis de componentes principales (PCA), pero siendo un análisis *supervisado*

- crea un modelo de regresión lineal proyectando las variables predichas y observables en un nuevo espacio
- muy adecuado para cuando existen más indicadores (compuestos) que observaciones (muestras)
- cada compuesto posee un *t-score* que representa su impacto en la predicción
- se asigna un valor de confianza de la predicción al ejecutar el modelo



# Análisis estadístico univariante y multivariante

The screenshot displays the MetaboAnalyst 3.5 web interface. The browser address bar shows the URL `www.metaboanalyst.ca/faces/upload/StatUploadView.xhtml`. The page title is "MetaboAnalyst -- a comprehensive tool for metabolomics analysis and interpretation".

**1) Upload your data**

Tab-delimited text (.txt) or comma-separated values (.csv) file:

Data Type:  Concentrations  Spectral bins  Peak intensity table

Format:

Data File:  DataMatrix.csv

Zipped Files (.zip) :

Data Type:  NMR peak list  MS peak list  MS spectra

Data File:  No se ha seleccionado ningún archivo.

Pair File:  No se ha seleccionado ningún archivo.

**2) Try our test data :**

Data Type	Description
-----------	-------------

**R Command History**

```
1. mSet<-InitDataObjects("pktable",
"stat", FALSE)
2. mSet<-Read.TextData(mSet,
"Replacing_with_your_file_path",
"colu", "disc");
3. mSet<-SanityCheckData(mSet)
```

Xia Lab @ McGill (last updated 2017-11-28)



# Predicción de clases: Validación del modelo

se evalúa la exactitud de la regla de predicción que se crea y proporciona una indicación de modelos de sobreajuste:

## dejando uno fuera (*leave one out*)

- se utilizan todas las muestras del conjunto de entrenamiento excepto una para construir la regla de predicción
- utilizando esta regla, se predice la clase de muestra que se ha dejado fuera
- la muestra se devuelve al conjunto de entrenamiento y se deja fuera una muestra diferente, volviendo a elaborar la regla de predicción con las muestras que quedan
- se repite este proceso hasta que se haya predicho cada muestra del conjunto de entrenamiento exactamente una vez
- se recuenta entonces el número de predicciones correctas e incorrectas para determinar el porcentaje de éxito

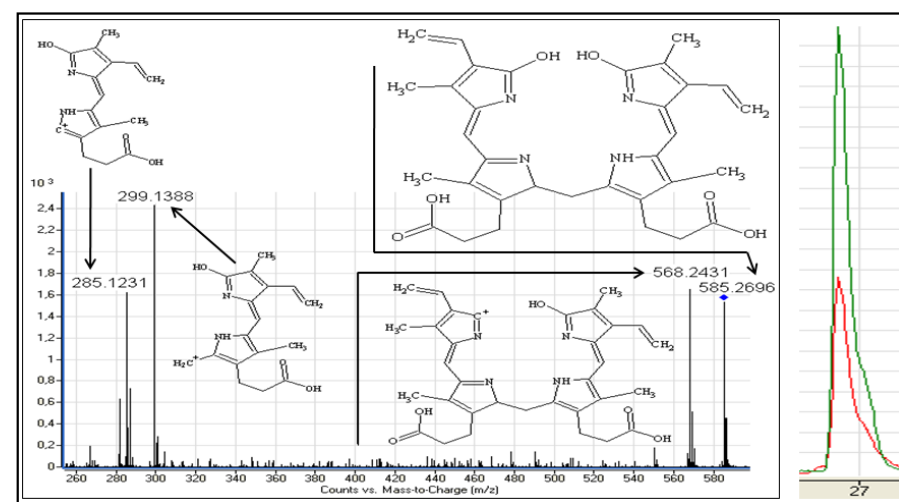
## $N$ - fold

1. las muestras del conjunto de entrenamiento se dividen aleatoriamente en  $N$  subconjuntos iguales, manteniendo una frecuencia de clases relativa
2.  $N-1$  subconjuntos se combinan entonces para el entrenamiento y el conjunto sobrante se utiliza para el ensayo
3. se repite paso a paso dejando un grupo fuera cada vez
4. se repite el paso 1, 2, 3  $M$  veces
5. cada muestra se predice  $M$  veces y se comunica la clase que haya sido predicha más veces a lo largo de esas  $M$  veces en los resultados de validación

# Identificación

1. Búsqueda en base de datos con medida de masa exacta
2. Búsqueda en base de datos comparando el **patrón isotópico**
3. Búsqueda en base de datos comparando el patrón isotópico y el **tiempo de retención**
4. Búsqueda en librerías de MS/MS
5. Búsqueda en librerías de MS/MS y **tiempo de retención**

Confianza



Search results table:

Compound Name	Precursor Ion	Collision Energy	Ion Polarity	Ionization Mode	Instrument Type
(-) Ibuprofen	203.26425	14.1	Negative	ESI	QTOF
Dienyl ethyl acetic acid	115.07645	10	ESI	ESI	QTOF
(-) Ibuprofen	203.26425	14.1	Negative	ESI	QTOF
(-) Ibuprofen	203.26425	14.1	Negative	ESI	QTOF
(-) Ibuprofen	203.26425	14.1	Negative	ESI	QTOF

Compound formula: C9H10N4O2S2

7 formula candidates from MFG:

ID	Formula	Score	Ref. Comp.	Weight
1	C9H10N4O2S2	100	3	100.0
2	C9H10N4O2S2	125	10	125.0
3	C9H10N4O2S2	11	14	6.3
4	C9H10N4O2S2	1	1	0.1

# CLASIFICACIONES DE BASES DE DATOS

- **Basadas datos espectrales**
  - Principalmente pequeñas moléculas y no solo metabolitos
  - NMR
  - MS o MS/MS
- **Basadas en información de compuestos**
  - Nombre de compuesto, estructuras, propiedades físicas, identificación
- **Basadas en base de datos de rutas metabólicas**
  - Rutas de metabolitos, xenobióticos, proteínas y de señalización
- **Base de datos metabolómica completa**
  - Una combinación de las anteriores

# Lista de Bases de Datos en 2018

Nombre	URL	Nombre	URL
	<a href="http://aralip.plantbiology.msu.edu/pathways/pathways">http://aralip.plantbiology.msu.edu/pathways/pathways</a>		
ARALIP	<a href="http://aralip.plantbiology.msu.edu/pathways/pathways">ays</a>	KEGG	<a href="http://prime.psc.riken.jp/?action=metabolites_index">http://prime.psc.riken.jp/?action=metabolites_index</a>
AtIPD	<a href="http://www.atipd.ethz.ch/">http://www.atipd.ethz.ch/</a>	KEGG Glycan	<a href="http://www.genome.jp/kegg/glycan/">http://www.genome.jp/kegg/glycan/</a>
BiGG	<a href="http://bigg.ucsd.edu/">http://bigg.ucsd.edu/</a>	KNAPSAcK	<a href="http://prime.psc.riken.jp/?action=metabolites_index">http://prime.psc.riken.jp/?action=metabolites_index</a>
BioCyc	<a href="http://biocyc.org/">http://biocyc.org/</a>	LipidMaps	<a href="http://www.lipidmaps.org/">http://www.lipidmaps.org/</a>
BioNumbers	<a href="http://bionumbers.hms.harvard.edu/">http://bionumbers.hms.harvard.edu/</a>	MarkerDB	<a href="http://www.markerdb.ca/users/sign_in">http://www.markerdb.ca/users/sign_in</a>
BML-NMR	<a href="http://www.bml-nmr.org/">http://www.bml-nmr.org/</a>	MassBank	<a href="http://www.massbank.jp/">http://www.massbank.jp/</a>
BioMagResBank	<a href="http://www.bmrwisc.edu/metabolomics/">http://www.bmrwisc.edu/metabolomics/</a>	MetaboAnalyst	<a href="http://www.metaboanalyst.ca/MetaboAnalyst/">http://www.metaboanalyst.ca/MetaboAnalyst/</a>
BMDB	<a href="http://www.cowmetdb.ca/cgi-bin/browse.cgi">http://www.cowmetdb.ca/cgi-bin/browse.cgi</a>	MetaboLights	<a href="http://www.ebi.ac.uk/metabolights/index">http://www.ebi.ac.uk/metabolights/index</a>
ChEBI	<a href="http://www.ebi.ac.uk/chebi/">http://www.ebi.ac.uk/chebi/</a>	MetaCrop	<a href="http://metacrop.ipk-gatersleben.de/apex/f?p=269:111:">http://metacrop.ipk-gatersleben.de/apex/f?p=269:111:</a>
ChEMBL	<a href="https://www.ebi.ac.uk/chembl/about#">https://www.ebi.ac.uk/chembl/about#</a>	MetaCyc	<a href="http://metacyc.org/">http://metacyc.org/</a>
ChEBI	<a href="http://www.ebi.ac.uk/chebi/">http://www.ebi.ac.uk/chebi/</a>	METAGENE	<a href="http://www.metagene.de/program/a.prg">http://www.metagene.de/program/a.prg</a>
ChemMine	<a href="http://chemminedb.ucr.edu/">http://chemminedb.ucr.edu/</a>	METLIN	<a href="https://metlin.scripps.edu/index.php">https://metlin.scripps.edu/index.php</a>
ChemSpider	<a href="http://www.chemspider.com/">http://www.chemspider.com/</a>	MMCD	<a href="http://mmcd.nmrfam.wisc.edu/">http://mmcd.nmrfam.wisc.edu/</a>
CCD	<a href="http://ccd.chemnetbase.com/intro/index.jsp#about">http://ccd.chemnetbase.com/intro/index.jsp#about</a>	mzCloud	<a href="https://mzcloud.org/">https://mzcloud.org/</a>
CSF Metabolome Database	<a href="http://www.csfmetabolome.ca/">http://www.csfmetabolome.ca/</a>	OMIM	<a href="http://www.ncbi.nlm.nih.gov/omim/">http://www.ncbi.nlm.nih.gov/omim/</a>
CyberCell Database	<a href="http://ccdb.wishartlab.com/CCDB/">http://ccdb.wishartlab.com/CCDB/</a>	OMMBID	<a href="http://ommbid.mhmedical.com/">http://ommbid.mhmedical.com/</a>
DrugBank	<a href="http://www.drugbank.ca/">http://www.drugbank.ca/</a>	Oryzabase	<a href="http://www.shigen.nig.ac.jp/rice/oryzabase/">http://www.shigen.nig.ac.jp/rice/oryzabase/</a>
ECMDB	<a href="http://www.ecmdb.ca/">http://www.ecmdb.ca/</a>	PepBank	<a href="http://pepbank.mgh.harvard.edu/">http://pepbank.mgh.harvard.edu/</a>
ExPaSy Pathways	<a href="http://web.expasy.org/pathways/">http://web.expasy.org/pathways/</a>	PharmGKB	<a href="http://www.pharmgkb.org/">http://www.pharmgkb.org/</a>
	<a href="http://fiehnlab.ucdavis.edu/Metabolite-Library-2007/">http://fiehnlab.ucdavis.edu/Metabolite-Library-2007/</a>		
Fiehn GC-MS Database	<a href="http://fiehnlab.ucdavis.edu/Metabolite-Library-2007/">2007/</a>	PMN	<a href="http://www.plantcyc.org/">http://www.plantcyc.org/</a>
FoodB	<a href="http://www.foodb.ca">http://www.foodb.ca</a>	PubChem	<a href="http://pubchem.ncbi.nlm.nih.gov/">http://pubchem.ncbi.nlm.nih.gov/</a>
GMDB	<a href="http://gmd.mpimp-golm.mpg.de/">http://gmd.mpimp-golm.mpg.de/</a>	Reactome	<a href="http://www.reactome.org/">http://www.reactome.org/</a>
HMDB	<a href="http://metabolomics.pharm.uconn.edu/iimdb/">http://metabolomics.pharm.uconn.edu/iimdb/</a>	RiceCyc	<a href="http://pathway.gemstone.org/gramene/ricecyc.shtml">http://pathway.gemstone.org/gramene/ricecyc.shtml</a>
HumanCyc	<a href="http://www.genome.jp/kegg/">http://www.genome.jp/kegg/</a>	Serum Metabolome Database	<a href="http://www.serummetabolome.ca/">http://www.serummetabolome.ca/</a>
IIDMB	<a href="http://www.genome.jp/kegg/glycan/">http://www.genome.jp/kegg/glycan/</a>	SetupX & BinBase	<a href="http://fiehnlab.ucdavis.edu/projects/binbase_setupx">http://fiehnlab.ucdavis.edu/projects/binbase_setupx</a>

CEU



Seleccionar archivo Ningún archivo seleccionado

**Experimental Masses (\*):** enter significant input masses

**Retention Times:** enter significant retention times

**Composite Spectra:** enter significant composite spectra

Seleccionar archivo Ningún archivo seleccionado

**All Experimental Masses:** enter all input masses

**All Retention Times:** enter all retention times

**All Composite Spectra:** enter all composite spectra

**Chemical Alphabet (\*):**  
All  
CHNOPS  
CHNOPS + Cl

**Modifiers (\*):**  
None  
NH3  
HCOO  
CH3COO  
HCOONH3  
CH3COONH3

**Databases (\*):**  
 All except MINE  
 All (Including In Silico Compounds)  
 Kegg  
 HMDB  
 LipidMaps  
 Metlin  
 MINE (Only In Silico Compounds)

**Metabolites (\*):**  
All except peptides  
Only lipids  
All including peptides

**Input Masses Mode (\*):**  
Neutral Masses  
m/z Masses

**Ionization Mode (\*):**  
Neutral  
Positive Mode  
Negative Mode  
calculation of new m/z from neutral mass based on selected adducts

**Adducts (\*):**  
 All  
 M+H  
 M+2H  
 M+Na  
 M+K  
 M+NH4

- Dedicado a la anotación de metabolitos.
- Realiza búsquedas en compuestos unificados de distintas fuentes.
- Aplica conocimiento basado en la información de entrada proporcionada por el usuario.
- Ayuda a identificar lípidos oxidados.
- <http://ceumass.eps.uspceu.es/mediator>



# CEU

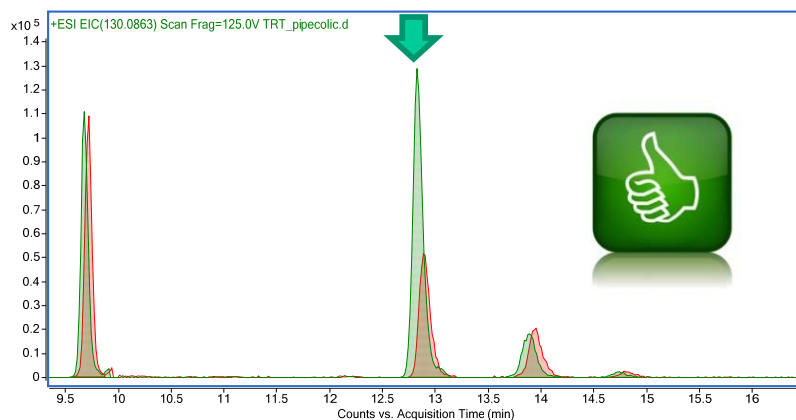


# MASS MEDIATOR

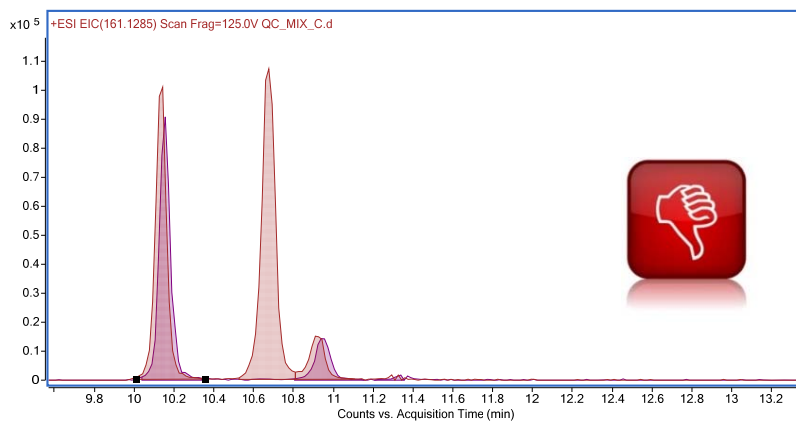
A	B	C	D	E	F	G	H	I	J	K	L	M	N	O		
1	LIST OF COMPOUNDS															
2	Experimental mass	Identifier	Adduct	PPM Err	Molecular Weigh	Name	Formula	CAS	Kegg	HMDB	LipidMaps	Metlin	PubChem	InChIKey	Pathways	
3	399.3367	17732	M-H	5	399.3349	L-palmitoylcarnitine	C23H45NO4				LMEFA07070079			XOMRRQKXKHMVMOC-NRFANRHFSA-N		
4	399.3367	17751	M-H	5	399.3349	O-palmitoylcarnitine	C23H45NO4				LMEFA07070098			XOMRRQKXKHMVMOC-UHFFFAOYSA-N		
5	399.3367	17657	M-H	5	399.3349	Palmitoylcarnitine	C23H45NO4	2364-67-2	C02390	HMDB0000222	LMEFA07070004	36667	11953816	XOMRRQKXKHMVMOC-OAQYLSRUS	Fatty acid Metabolism Fatty a	
6	399.3367	0	M-Na	0	No compounds found for experimental mass 399.3367 and adduct: I											
7	399.3367	13442	M-NH4	5	382.3083	methyl 9-butylperoxy-10,12-octadecadienoate	C23H42O4				LMEFA01040036	74461		XVZNFQXKMPCH-ZIAPIVEJSA-N		
8	399.3367	13443	M-NH4	5	382.3083	methyl 13-butylperoxy-9,11-octadecadienoate	C23H42O4				LMEFA01040037	74462		GUVYTNFTPALBOJ-AEPWDTSSA-N		
9	399.3367	95769	M-NH4	5	382.3083	Lepidumterpenyl ester	C23H42O4				HMDB0036865	31868	11734320	PASMASQJCDKBJK-UHFFFAOYSA-N		
10	399.3367	53861	M-NH4	5	382.3083	MG(0.0/20.2(11Z,14Z)/0.0)	C23H42O4				HMDB0011544	62328	53480964	PMJSUEZTCFTBMD-HZJYTRNSA-N		
11	399.3367	52646	M-NH4	5	382.3083	MG(20.2(11Z,14Z)/0.0/0.0)	C23H42O4				HMDB0011574	62356	53480983	QRBGFYBOCBYOSN-KDTZJXJHSA-N		
12	399.3367	80631	M-NH4	5	382.3083	Persenone B	C23H42O4				HMDB0035955	31145		NLXNQLZUQMHHEB-ISLRYVAYSAN		
13	399.3367	0	M-H-H2O	0	No compounds found for experimental mass 399.3367 and adduct: I											
14	421.3169	16968	M-H	6	421.3192	Gamma-linolengl carnitine	C25H43NO4				HMDB0006318	LMEFA07010893	58389	53477819	YDPMHMLMYSAQK-BAHSRKMSSA-N	
15	421.3169	96332	M-H	6	421.3192	Alpha-linolengl carnitine	C25H43NO4				HMDB0006319		58390	53477821	DFVGGGHKDAHYIU-UHMZJMFSA-N	
16	421.3169	126612	M-H	9	421.3205	AGELASINE	C26H39N5						43731			
17	421.3169	138401	M-H	9	421.313	Latanoprost ethyl amide-d4	C25H35D4NO4						36571			
18	421.3169	17732	M-Na	0	399.3349	L-palmitoylcarnitine	C23H45NO4				LMEFA07070079			XOMRRQKXKHMVMOC-NRFANRHFSA-N		
19	421.3169	17751	M-Na	0	399.3349	O-palmitoylcarnitine	C23H45NO4				LMEFA07070098			XOMRRQKXKHMVMOC-UHFFFAOYSA-N		
20	421.3169	17657	M-Na	0	399.3349	Palmitoylcarnitine	C23H45NO4	2364-67-2	C02390	HMDB0000222	LMEFA07070004	36667	11953816	XOMRRQKXKHMVMOC-OAQYLSRUS	Fatty acid Metabolism Fatty a	
21	421.3169	1294	M-NH4	6	404.2927	1alpha,25-dihydroxy-21-nor-20-oxavitamin D3 / 1alpha,25-dihydroxy-2	C25H40O4				LMST03020029	41970		AOMQZQKQVZ2TNY-OQGZSIESA-N		
22	421.3169	1295	M-NH4	6	404.2927	1alpha,25-dihydroxy-24-nor-22-oxavitamin D3 / 1alpha,25-dihydroxy-2	C25H40O4				LMST03020030	41971		UMRLCGLUMINBCT-NPMXOCSOSA-N		
23	421.3169	2650	M-NH4	6	404.2927	7b-Hydroxy-3-oxo-5b-eholan-24-oate	C25H40O4				LMST04070028	57339		XHRLTYUHWGHDJ-JFRFJXPMNSA-N		
24	421.3169	117990	M-NH4	6	404.2927	Androstane-3,17-diol dipropionate,5alpha-Androstane-3alpha,17beta	C25H40O4	4350-14-5	C14624			70213	134572	FWAYUWSHYLKUEY-LFYVYRBCSA-N		
25	421.3169	86607	M-NH4	6	404.2927	11-Carboxy-gamma-chromanol	C25H40O4				HMDB0012517		53481453	IITULCNMOMXAH-YUULODDPSA-N		
26	421.3169	89679	M-NH4	6	404.2927	MG(0.0/22.5(7Z,10Z,13Z,16Z,19Z)/0.0)	C25H40O4				HMDB0011556	62339	53480971	LRBJLYDLUADN-JLNKQISISA-N		
27	421.3169	50261	M-NH4	6	404.2927	MG(22.5(4Z,7Z,10Z,13Z,16Z)/0.0/0.0)	C25H40O4				HMDB0011585	62367	53480993	HDIQCISTZKHUDD-AJWITYRPSA-N		
28	421.3169	105373	M-NH4	6	404.2927	MG(0.0/22.5(4Z,7Z,10Z,13Z,16Z)/0.0)	C25H40O4				HMDB0011555	62338	53480970	NPZVSBAEZLZYQU-WMPRHZDHSAN		
29	421.3169	56824	M-NH4	6	404.2927	MG(22.5(7Z,10Z,13Z,16Z,19Z)/0.0/0.0)	C25H40O4				HMDB0011586	62368	53480994	IDSLCYURGAOTDA-YAWQMQZOFSA-N		
30	421.3169	17695	M-H-H2O	5	439.3298	3-hydroxylinoleoylcarnitine	C25H45NO5				LMEFA07070042			WGYXCASYXFNHSI-UTJQPWESSAN		
31	315.2424	17712	M-H	5	315.241	Decanoylcarnitine	C17H33NO4				HMDB0000651	LMEFA07070059	10245190		LZOSYCMHQXPBFU-UHFFFAOYSA-N	
32	315.2424	126591	M-H	5	315.241	L-Hexanoylcarnitine n-butyl ester	C17H33NO4					3549				
33	315.2424	17659	M-H	5	315.241	O-decanoyl-R-carnitine	C17H33NO4	3992-45-8	C03299	HMDB0062631	LMEFA07070006	36669	11953821	LZOSYCMHQXPBFU-OAHLLOKOSAN		
34	315.2424	0	M-Na	0	No compounds found for experimental mass 315.2424 and adduct: I											
35	315.2424	14277	M-NH4	5	298.2144	8E-Heptadecenedioic acid	C17H30O4				LMEFA01170053	74925		VDTSYDDUGXHLDY-OVQJBTEDSAN		
36	315.2424	11819	M-NH4	5	298.2144	Plakortinc acid	C17H30O4				C17158	71590	10402441	ZCLJFHUIADAYRQ-CMDGGGBGSA-N		
37	315.2424	0	M-H-H2O	0	No compounds found for experimental mass 315.2424 and adduct: I											
38	337.2234	0	M-H	0	No compounds found for experimental mass 337.2234 and adduct: I											
39	337.2234	17712	M-Na	2	315.241	Decanoylcarnitine	C17H33NO4				HMDB0000651	LMEFA07070059	10245190		LZOSYCMHQXPBFU-UHFFFAOYSA-N	
40	337.2234	126591	M-Na	2	315.241	L-Hexanoylcarnitine n-butyl ester	C17H33NO4					3549				
41	337.2234	17659	M-Na	2	315.241	O-decanoyl-R-carnitine	C17H33NO4	3992-45-8	C03299	HMDB0062631	LMEFA07070006	36669	11953821	LZOSYCMHQXPBFU-OAHLLOKOSAN		
42	337.2234	1060	M-NH4	6	320.1988	testolic acid	C19H28O4				C01618	LMST02020081	57817	439534	KMUJXIPRPXRP-PT-DZBHQSCQSA-N	
43	337.2234	116962	M-NH4	6	320.1988	10beta-Hydroxy-6beta-isobutyrylforanoceremophilane	C19H28O4				C09685		67884	442377	WVBNALQGLGJMUUJ-BIGGFVEDSAN	
44	337.2234	130809	M-NH4	6	320.1988	(+)-alpha-CMBHC	C19H28O4	7083-09-2				44834				
45	337.2234	53386	M-NH4	6	320.1988	[8]-Gingerdione	C19H28O4	77334-06-6			HMDB0033276	33864	14440537	QDSRAFNZQKMPZ-UHFFFAOYSA-N		
46	337.2234	47665	M-NH4	6	320.1988	5-Carboxy-alpha-chromanol	C19H28O4				HMDB0012738		53481524	QVPMILVBAFZJBMIMEVZPHKSA-N		



# Confirmación mediante Adición estándar



Ácido pipercolico

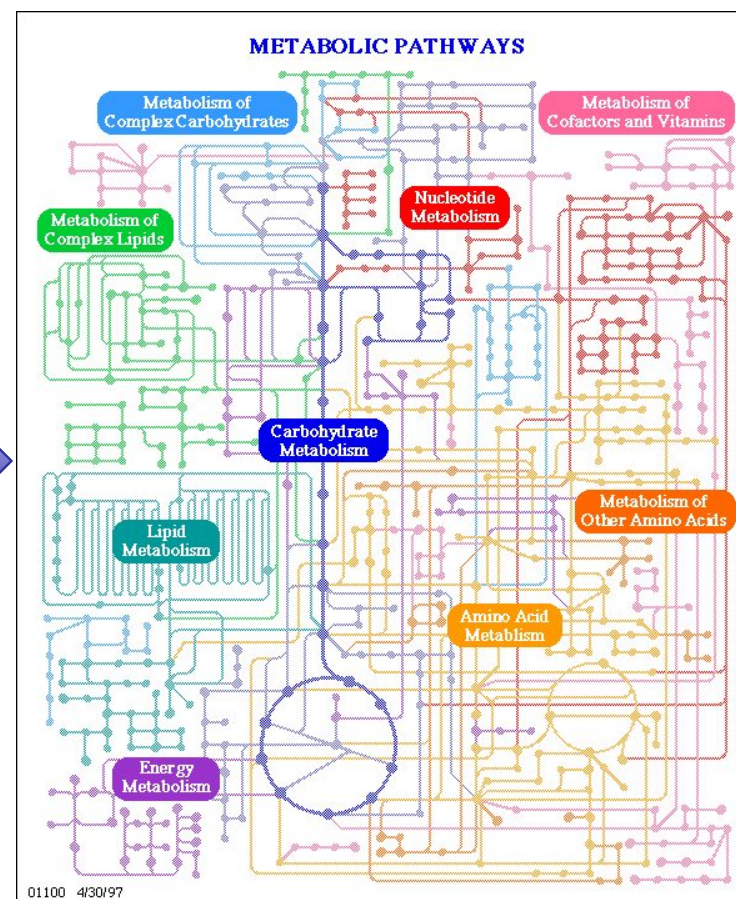
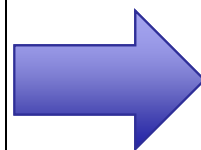


Metil-lisina

# De Listas a Rutas

## metabolómica

Compound	Retention Time (min)	Conc. in Urine (µM)	Compound	Retention Time (min)	Conc. in Urine (µM)
Dns-o-phospho -L-serine	0.92	<D.L.*	Dns-Ile	6.35	25
Dns-o-phospho -L-tyrosine	0.95	<D.L.	Dns-3-aminosalicylic acid	6.44	0.5
Dns-adenosine monophosphate	0.99	<D.L.	Dns-pipecolic acid	6.50	0.5
Dns-o-phosphoethanolamine	1.06	16	Dns-Leu	6.54	54
Dns-glucosamine	1.06	22	Dns-cystathionine	6.54	0.3
Dns-o-phospho -L-threonine	1.09	<D.L.	Dns-Leu-Pro	6.60	0.4
Dns-6-dimet hylamine purine	1.20	<D.L.	Dns-5-hydroxylysine	6.65	1.6
Dns-3-methyl -histidine	1.22	80	Dns-Cystine	6.73	160
Dns-aurine	1.25	834	Dns-N-norleucine	6.81	0.1
Dns-carnosine	1.34	28	Dns-5-hydroxydopamine	7.17	<D.L.
Dns-Arg	1.53	36	Dns-dimethylamine	7.33	293
Dns-Asn	1.55	133	Dns-5-HIAA	7.46	18
Dns-hypotaurine	1.58	10	Dns-umbelliferone	7.47	1.9
Dns-homocarnosine	1.61	3.9	Dns-2,3 -diam inopropionic acid	7.63	<D.L.
Dns-guanidine	1.62	<D.L.	Dns-L-ornithine	7.70	15
Dns-Gln	1.72	633	Dns-4-acetyamidophenol	7.73	51
Dns-allantoin	1.83	3.8	Dns-procaine	7.73	8.9
Dns-L-citrulline	1.87	2.9	Dns-homocystine	7.76	3.3
Dns-1 (or 3 -)-methylhistamine	1.94	1.9	Dns-acetaminophen	7.97	82
Dns-adenosine	2.06	2.6	Dns-Phe-Phe	8.03	0.4
Dns-methylguanidine	2.20	<D.L.	Dns-5-methyo xysalicylic acid	8.04	2.1
Dns-Ser	2.24	511	Dns-Lys	8.16	184
Dns-aspartic acid amide	2.44	26	Dns-aniline	8.17	<D.L.
Dns-4-hydroxy -proline	2.56	2.3	Dns-leu-Phe	8.22	0.3
Dns-Glu	2.57	21	Dns-His	8.35	1550
Dns-Asp	2.60	90	Dns-4-thialysine	8.37	<D.L.
Dns-Thr	3.03	157	Dns-benzylamine	8.38	<D.L.
Dns-ephedrine	3.05	<D.L.	Dns-1-ephedrine	8.50	0.6
Dns-ethanolamine	3.11	471	Dns-tryptamine	8.63	0.4
Dns-aminoadipic acid	3.17	70	Dns-pyridoxamine	8.94	<D.L.
Dns-Gly	3.43	2510	Dns-2-methyl -benzylamine	9.24	<D.L.
Dns-Ala	3.88	593	Dns-5-hydroxytrptophan	9.25	0.12
Dns-aminolevulinic acid	3.97	30	Dns-1,3-diaminopropane	9.44	0.23
Dns-r-amino -butyric acid	3.98	4.6	Dns-putrescine	9.60	0.5
Dns-p-amino -hippuric acid	3.98	2.9	Dns-1,2-diaminopropane	9.66	0.1
Dns-5-hydro xymethyluril	4.58	1.9	Dns-tyrosinamide	9.79	29
Dns-tryptophanamide	4.70	5.5	Dns-dopamine	10.08	140
Dns-isoguanine	4.75	<D.L.	Dns-cadaverine	10.08	0.08
Dns-5-aminopentanoic acid	4.79	1.6	Dns-histamine	10.19	0.4
Dns-sarcosine	4.81	7.2	Dns-3-methoxy -tyr amine	10.19	9.2
Dns-3-amino -isobutyrate	4.81	85	Dns-Tyr	10.28	321
Dns-2-aminobutyric acid	4.91	17	Dns-cysteamine	10.44	<D.L.



# Bases de datos de rutas metabólicas

- Excelente fuente de datos biológicos que sirve para relacionar metabolitos con genes, proteínas y enfermedades, señalando eventos y procesos
- Ofrece distintas herramientas que permiten la visualización y el mapeo de genes/metabolitos
- Normalmente cubre múltiples especies
- KEGG ([www.genome.jp/kegg/](http://www.genome.jp/kegg/)), BioCyc/MetaCyc (<https://biocyc.org/>), SMPDB ([www.smpdb.ca](http://www.smpdb.ca)), Reactome ([www.reactome.org](http://www.reactome.org)), WikiPathways (<http://www.wikipathways.org>)...
- «*De forma estricta, se podría afirmar que no existen las rutas metabólicas... son solo redes.*» (WikiPathways.org)

# KEGG – Enciclopedia de Genes y Genomas de Kioto

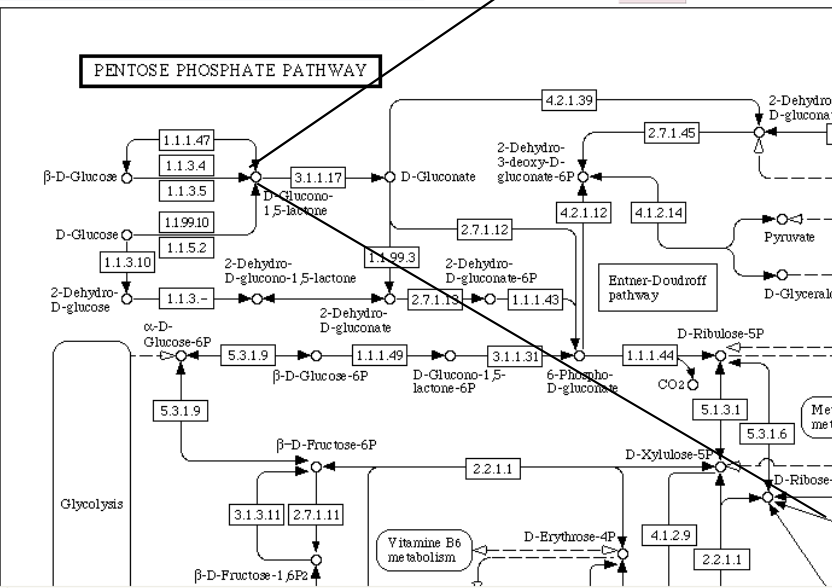
**Pentose phosphate pathway - Reference pathway - Microsoft Internet Explorer**

Address: <http://www.genome.jp/kegg/pathway/map/map00030.html>

**KEGG Pentose phosphate pathway - Reference pathway**

[ Pathway menu | Ortholog table ]

Reference pathway  Current selection



**DBGET Result: COMPOUND C00198 - Microsoft Internet Explorer**

Address: [http://www.genome.jp/dbget-bin/www\\_bget?compound+C00198](http://www.genome.jp/dbget-bin/www_bget?compound+C00198)

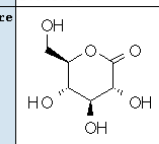
**KEGG COMPOUND: C00198**

Entry: C00198 Compound

Name: D-glucono-1,5-lactone; Gluconic lactone; Gluconic acid lactone; 1,5-gluconolactone; delta-Gluconolactone; D-gluconolactone; Glucarolactone; D-Aldonolactone; D-threo-Aldono-1,5-lactone

Formula: C<sub>6</sub>H<sub>10</sub>O<sub>6</sub>

Mass: 178.0478

Structure: 

C00198

Mol file KCF file DB search

Reaction: R00300 R00305 R00874 R01519 R01520 R01521 R01522 R02847 R03861 R06620

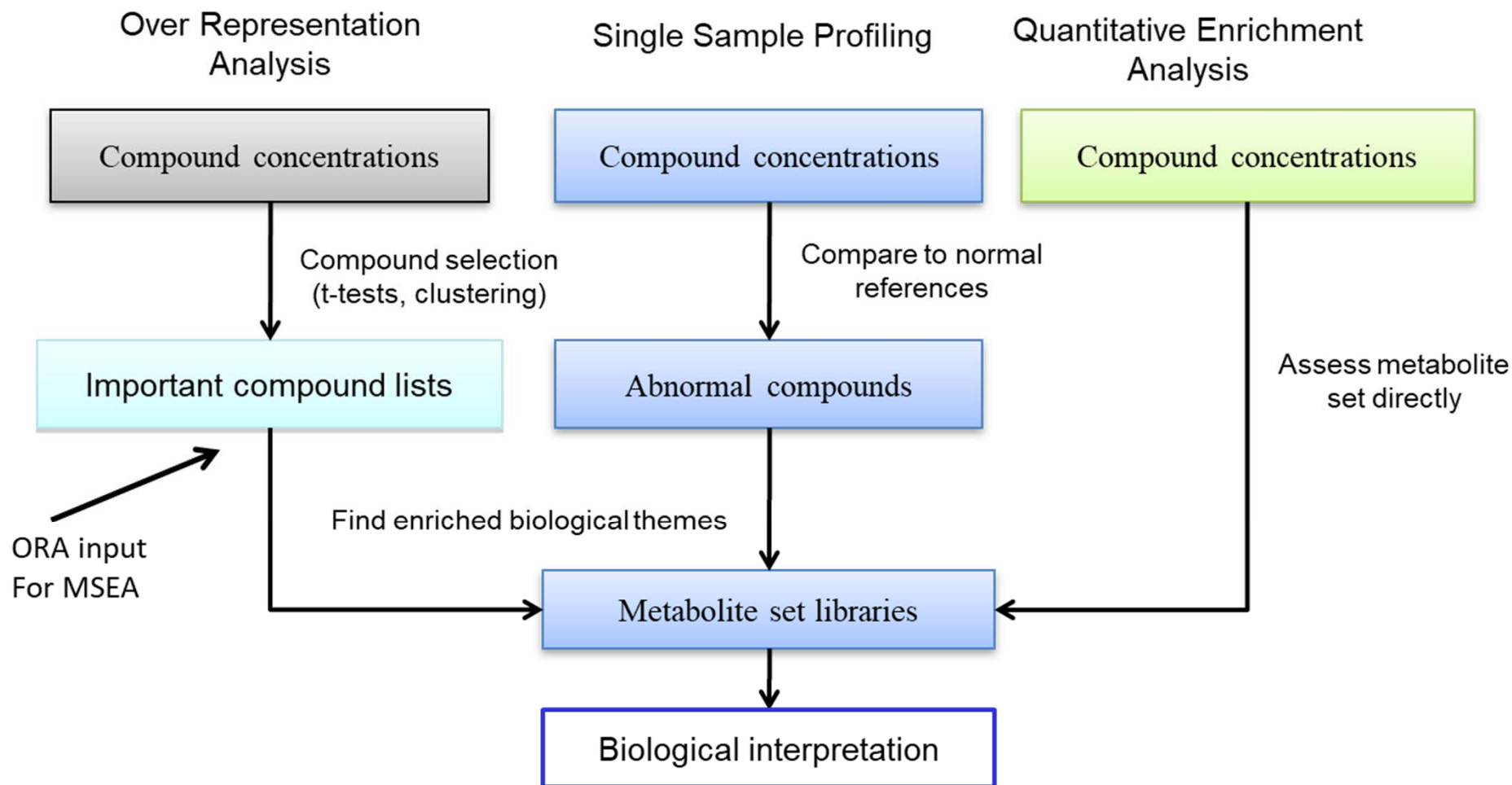
Pathway: PATH: map00030 Pentose phosphate pathway

Enzyme	1.1.1.47	1.1.1.118	1.1.1.121	1.1.3.4
	1.1.3.5	1.1.5.2	1.1.99.10	1.1.99.28
	2.2.1.122	2.2.1.173	2.2.1.17	

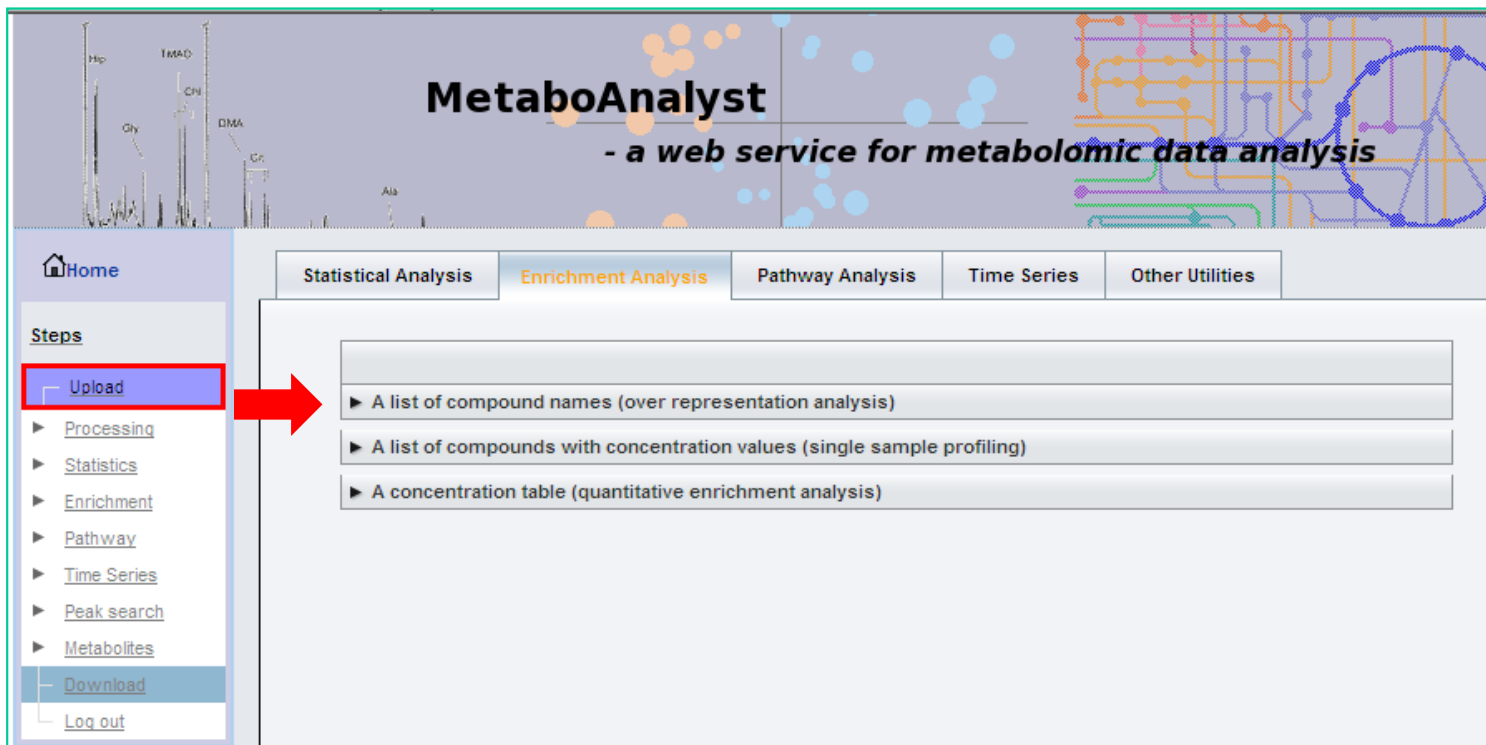
9:49 PM

<http://www.genome.jp/kegg/>

# El enfoque MSEA (*Metabolite Set Enrichment Analysis*)



# Empezar con una lista de compuestos



**MetaboAnalyst**  
- a web service for metabolomic data analysis

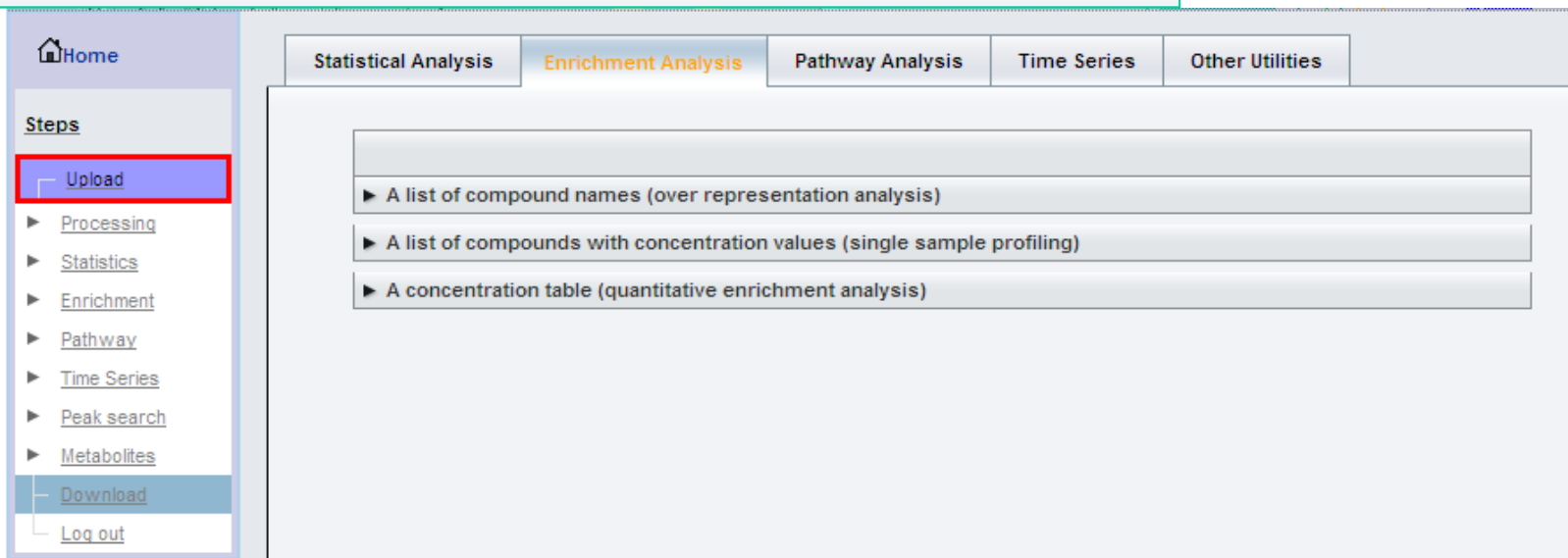
Home

Steps

- Upload
- Processing
- Statistics
- Enrichment
- Pathway
- Time Series
- Peak search
- Metabolites
- Download
- Log out

Statistical Analysis Enrichment Analysis Pathway Analysis Time Series Other Utilities

- A list of compound names (over representation analysis)
- A list of compounds with concentration values (single sample profiling)
- A concentration table (quantitative enrichment analysis)



Home

Steps

- Upload
- Processing
- Statistics
- Enrichment
- Pathway
- Time Series
- Peak search
- Metabolites
- Download
- Log out

Statistical Analysis Enrichment Analysis Pathway Analysis Time Series Other Utilities

- A list of compound names (over representation analysis)
- A list of compounds with concentration values (single sample profiling)
- A concentration table (quantitative enrichment analysis)



# Comparación con la concentración










Home


Steps

- Upload
- Processing
  - Pre-process
  - Name check
  - Conc. check**
  - Data check
  - Missing value
  - Data filter
  - Data editor
  - Color picker
  - Normalization
- Statistics
- Enrichment
- Pathway
- Time Series
- Peak search
- Metabolites
- Download
- Log out

## Comparison with Reference Concentration

Note: *reference concentrations* are in the form of **mean(min - max)** format. In cases where the ranges were not reported in the original literature, the min and max were calculated using the 95% confidence intervals. In the *Comparison* column, **H, M, L** means **higher, medium (within range), lower** compared to the reference concentrations. Click the **Image Icon** link to see a graphical summary for the comparisons.

Compound	Concentration	Reference Concentrations	Comparison	Detail	Include
L-Isoleucine	0.34	1.579 (0.789 - 2.368); 0.94 (0.27 - 1.61); 3.75 (1 - 6.5); 3 (1.5 - 4.5); 1.8 (0.8 - 2.8)	M		<input type="checkbox"/>
Fumaric acid	0.47	10.4 (2.8 - 53.7); 0.5 (0.1 - 1.7); 1 (0 - 2); 0.95 (0.02 - 1.88); 0.8 (0.1 - 1.7); 10.7 (0.1 - 28.2); 4.8 (0 - 35.2); 5 (1 - 33.5)	M		<input type="checkbox"/>
Acetone	0.58	4.2 (0.98 - 15.3); 0.92 (0.2 - 2.8); 320 (103 - 1290); 20 (2 - 180); 15.3 (2 - 120)	M		<input type="checkbox"/>
Succinic acid	9.4	14.4 (9.5 - 19.3); 3.8 (1.25 - 6.7); 12.6 (0.47 - 24.73); 14.48 (11.28 - 17.68); 9.9 (4.9 - 14.9); 39 (37 - 41); 197.2 (29.4 - 486.2); 185.4 (6 - 342.6); 7.7 (1.9 - 20); 11.6 (4 - 27.3); 8.25 (0.5 - 16)	M		<input type="checkbox"/>
1-Methylhistidine	9.6	2.3 (0 - 7.4); 33.6 (0 - 70); 28.1 (0 - 59.9); 30 (0 - 73); 45.5 (3.9 - 87.1); 1.3 (0 - 4.06); 4.6 (1.9 - 7.3); 46.1 (0 - 99.6); 15.9 (0 - 35.4)	M		<input type="checkbox"/>
L-Asparagine	19.62	35 (16.4 - 57.2); 9.211 (3.289 - 15.1); 0.96 (0.31 - 1.61); 10 (4.6 - 16.32)	M		<input type="checkbox"/>
3-Methylhistidine	9.7	42.76 (19.92 - 65.6); 15.1 (3.9 - 26.3); 12.5 (8.3 - 16.7)	M		<input type="checkbox"/>
L-Threonine	93.19	36.2 (10.82 - 61.58); 12.7 (4.934 - 20.4); 1 (0.16 - 2.4); 4.9 (2.4 - 7.4); 16 (7 - 25); 18 (8.4 - 27.6)	H		<input checked="" type="checkbox"/>
Creatine	720	46 (9 - 135); 113 (0 - 654); 26 (5 - 95); 167 (124 - 210); 212 (0 - 5000); 450 (0 - 10000)	M		<input type="checkbox"/>



# Análisis de Enriquecimiento Cuantitativo

## (Quantitative enrichment analysis)

Home

Statistical Analysis **Enrichment Analysis** Pathway Analysis Time Series Other Utilities

Steps

- Upload**
- Processing
- Statistics
- Enrichment
- Pathway
- Time Series
- Peak search
- Metabolites
- Download
- Log out

A list of compound names (over representation analysis)

A list of compounds with concentration values (single sample profiling)

**A concentration table (quantitative enrichment analysis)**

**Upload your concentration data (.csv)**

[Format](#)

Compound Label Type:

Phenotype Label:

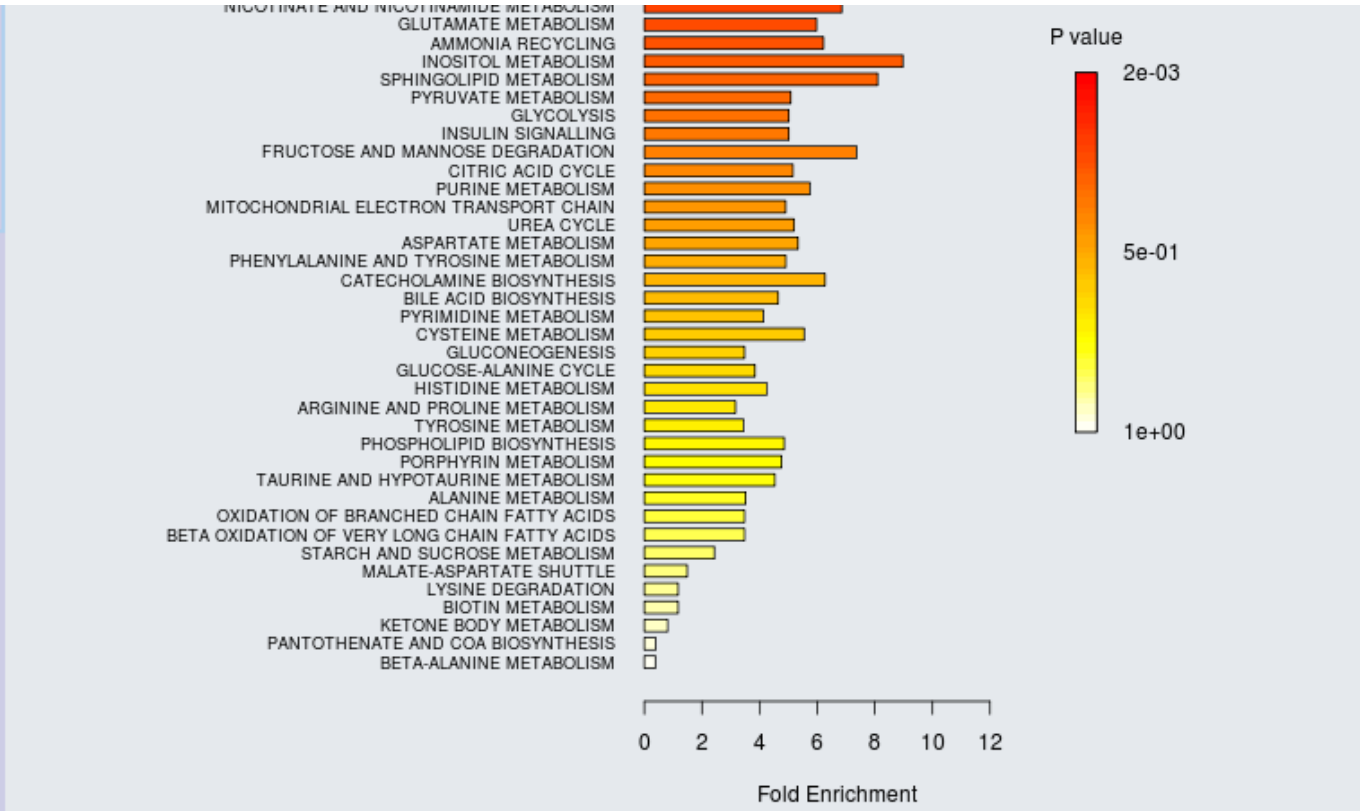
---





**Try our test data:**

Data	Compound	Phenotype	Description
<input checked="" type="radio"/> <a href="#">Data 1</a>	Common name	Discrete	Urinary metabolite concentrations from 77 cancer patients measured by 1H NMR. Phenotype: <b>N</b> - cachexic; <b>Y</b> - control
<input type="radio"/> <a href="#">Data 2</a>	PubChem CID	Continuous	Urinary metabolite concentrations from 97 cancer patients measured by 1H NMR. Phenotype: <b>muscle gain</b> (percentage within 100 days, negative values indicate muscle loss)

# RESULTADO

- ▶ [Time Series](#)
- ▶ [Peak search](#)
- ▶ [Metabolites](#)
- └─ [Download](#)
- └─ [Log out](#)



Metabolite Set	Total	Hit	Statistic	Expected	P Value	Holm P	FDR	Details
<b>TRYPTOPHAN METABOLISM</b>	34	2	15.088	1.3158	5.3712E-5	0.0024707	0.0020529	
<b>PROPANOATE METABOLISM</b>	18	1	17.695	1.3158	1.3942E-4	0.0062741	0.0020529	
<b>BETAINE METABOLISM</b>	10	2	14.311	1.3158	1.4515E-4	0.0063865	0.0020529	
<b>METHIONINE METABOLISM</b>	24	4	11.386	1.3158	1.7852E-4	0.0076762	0.0020529	



# Metaboanalyst

## Metabolic Pathway Analysis (MetPA)

- Objetivo: extender y potenciar el MSEA para rutas metabólicas mediante
  - La consideración de las **estructuras de ruta metabólicas**
  - La visualización dinámica de las rutas metabólicas
- Actualmente admite aprox. 1500 rutas que comprenden 17 organismos (basadas en KEGG)

# SESIÓN PRÁCTICA. VISUALS\_1



## Workflow4metabolomics



### Main menu

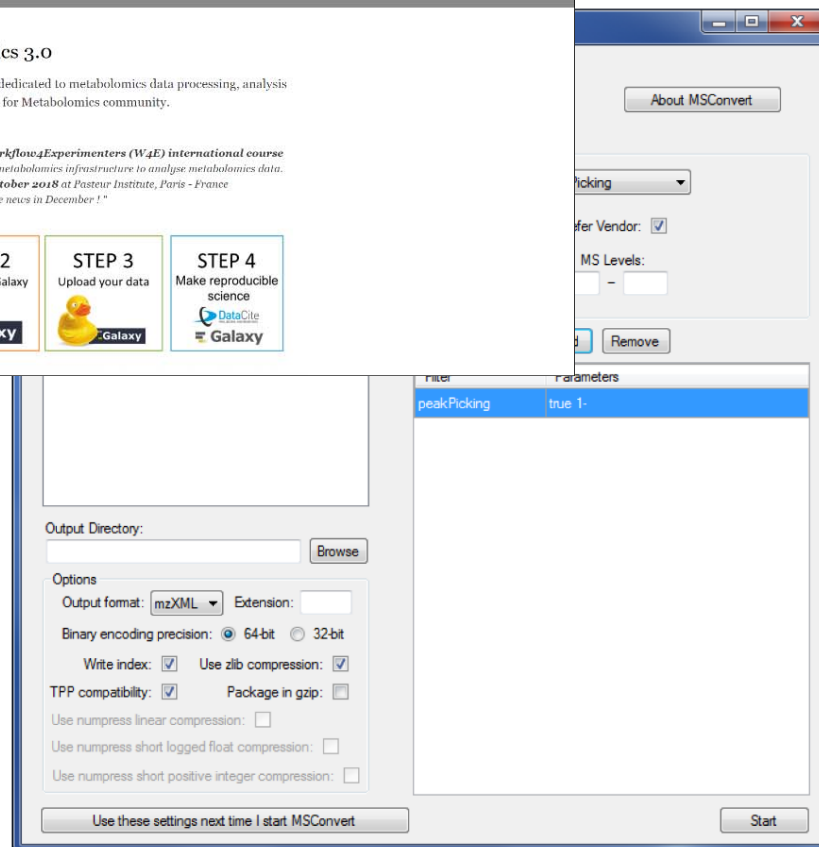
- Home
- Events
- History
- Introduction
  - The Galaxy environment
  - The LC-MS workflow
  - The GC-MS workflow
  - The NMR workflow
  - References
- HowTo
- Download
  - Datasets
- Referenced Workflows and Histories
- How to contribute?
- Developer resources
  - Source code
  - Virtual environments
- People
- Publications

### Workflow4Metabolomics 3.0

Welcome to the collaborative portal dedicated to metabolomics data processing, analysis and annotation for Metabolomics community.

"We are happy to announce the next **Workflow4Experimenters (W4E) international course 2018: Using Galaxy and the Workflow4metabolomics infrastructure to analyse metabolomics data.** Please save the date: **8-12 October 2018** at Pasteur Institute, Paris - France. More news in December!"

<b>STEP 1</b> Request an account 	<b>STEP 2</b> Connect to Galaxy 	<b>STEP 3</b> Upload your data 	<b>STEP 4</b> Make reproducible science 
--	---	--	---



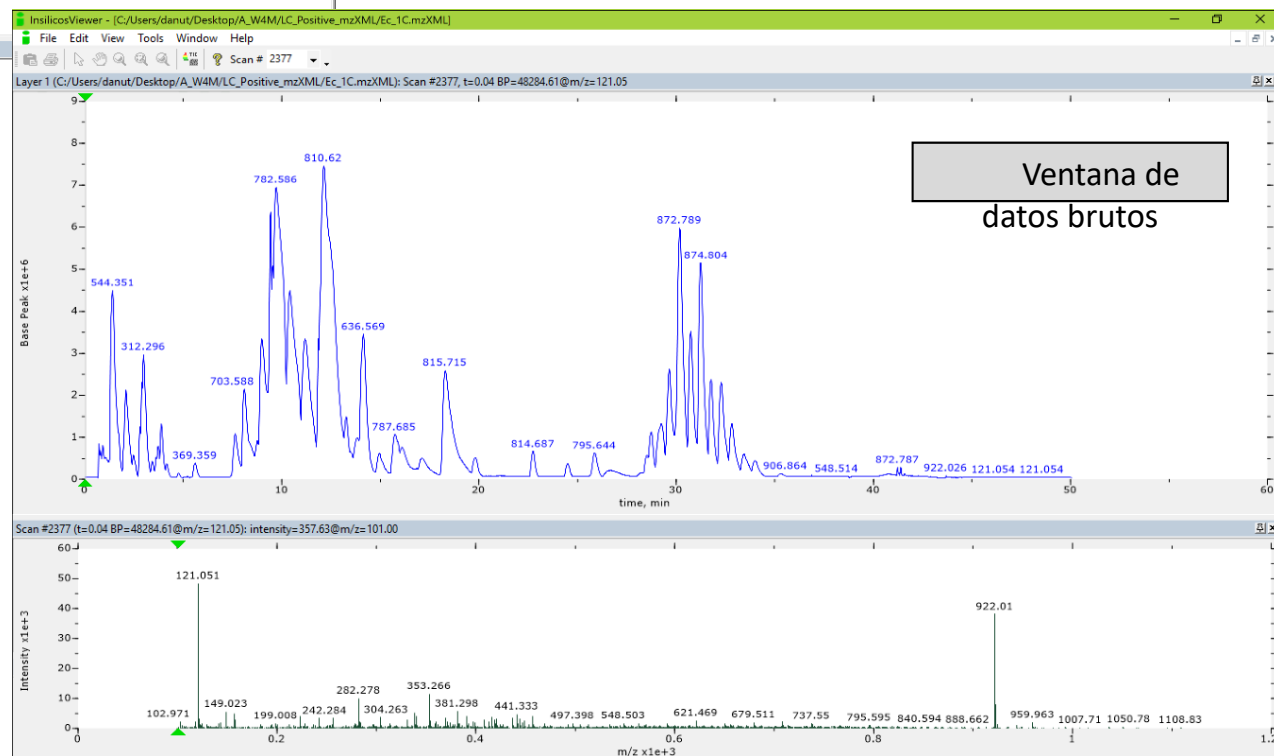
The screenshot shows the MSConvert application window. At the top, there is an "About MSConvert" button. Below it, there is a "Filter" dropdown menu set to "peakPicking" and a "Remove" button. The "MS Levels" section shows a value of "-". The "Output Directory" field is empty with a "Browse" button. The "Options" section includes: "Output format" set to "mzXML", "Extension" field, "Binary encoding precision" set to "64-bit", "Write index" checked, "Use zlib compression" checked, "TPP compatibility" checked, and "Package in gzip" unchecked. There are also three unchecked options for numpress compression. At the bottom, there is a "Start" button and a checkbox for "Use these settings next time I start MSConvert".

# SESIÓN PRÁCTICA. VISUALS\_2

The screenshot shows the InsilicosViewer application window. The menu bar includes File, Edit, View, Tools, Window, and Help. The 'File' menu is open, showing options like New, Open..., Close, Print..., Print Preview, Print Setup..., and Exit. The main area displays the 'licos Life Science Software' logo. A file list window is open, showing a directory named 'LC\_Positive\_mzXML' with a table of files:

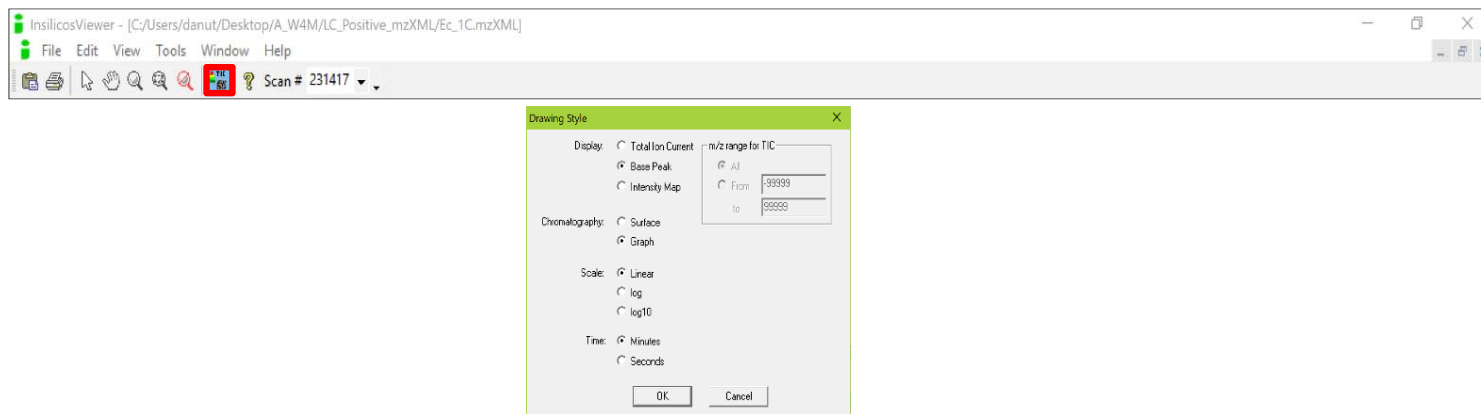
Nazwa	Data modyfikacji	Typ
Ec_1C	19.4.17 13:47	mass spec
Ec_2C	19.4.17 13:49	mass spec
Ec_3C	19.4.17 13:49	mass spec
Ec_4C	19.4.17 13:50	mass spec
Ec_5C	19.4.17 13:50	mass spec
Ec_6C	19.4.17 13:50	mass spec
Ec_7C	19.4.17 13:50	mass spec
Ec_8C	19.4.17 13:51	mass spec
Ec_9HC	19.4.17 13:51	mass spec
Ec_10HC	19.4.17 13:43	mass spec
Ec_11HC	19.4.17 13:43	mass spec
Ec_12HC	19.4.17 13:44	mass spec
Ec_13HC	19.4.17 13:44	mass spec
Ec_14HC	19.4.17 13:45	mass spec
Ec_15HC	19.4.17 13:45	mass spec

Below the list, there are fields for 'Nazwa pliku:' (set to 'Ec\_1C') and 'Pliki typu:' (set to 'MS Data Files (\*.mzXML;\*.mzData;\*.mzML;\*.RA)'), along with 'Otwórz' and 'Anuluj' buttons.





# SESIÓN PRÁCTICA. VISUALS\_3



Main menu

- Home
- Events
- History
- Introduction
  - The Galaxy environment
  - The LC-MS workflow
  - The GC-MS workflow
  - The NMR workflow
  - References
- HowTo
- Download
  - Datasets
  - Referenced WorkFlows and Histories
  - How to contribute?
- Developer resources
  - Source code
  - Virtual environments
- People
- Publications

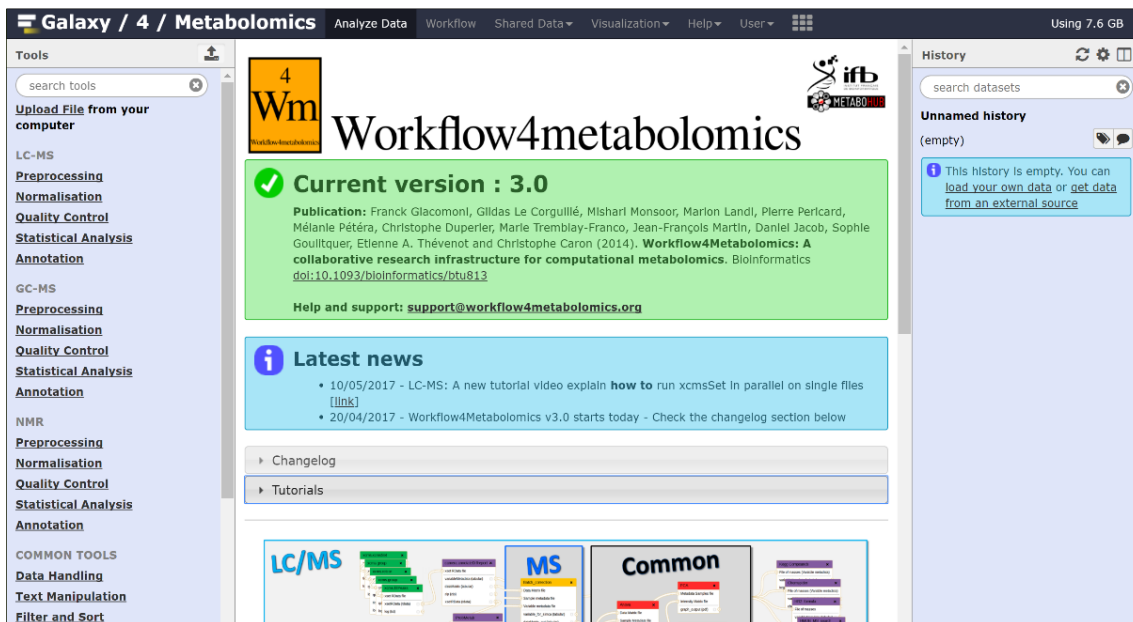
## Workflow4Metabolomics 3.0

Welcome to the collaborative portal dedicated to metabolomics data processing, analysis and annotation for Metabolomics community.

*"We are happy to announce the next **Workflow4Experimenters (W4E) international course 2018: Using Galaxy and the Workflow4metabolomics infrastructure to analyse metabolomics data.** Please save the date: **8-12 October 2018** at Pasteur Institute, Paris - France. More news in December!"*

<b>STEP 1</b> Request an account 	<b>STEP 2</b> Connect to Galaxy 	<b>STEP 3</b> Upload your data 	<b>STEP 4</b> Make reproducible science 
--	---	--	---

# SESIÓN PRÁCTICA. VISUALS\_4



Galaxy / 4 / Metabolomics Analyze Data Workflow Shared Data Visualization Help User Using 7.6 GB

Tools

search tools

Upload File from your computer

LC-MS

Preprocessing  
Normalisation  
Quality Control  
Statistical Analysis  
Annotation

GC-MS

Preprocessing  
Normalisation  
Quality Control  
Statistical Analysis  
Annotation

NMR

Preprocessing  
Normalisation  
Quality Control  
Statistical Analysis  
Annotation

COMMON TOOLS

Data Handling  
Text Manipulation  
Filter and Sort

4 Wm Workflow4metabolomics

ifb METABOLOMICS

Current version : 3.0

Publication: Franck Glacomoni, Gildas Le Corguillé, Mishari Monsoor, Marion Landi, Pierre Pericard, Mélanie Pétéra, Christophe Duperter, Marie Tremblay-Franco, Jean-François Martin, Daniel Jacob, Sophie Goulltquer, Etienne A. Thévenot and Christophe Caron (2014). **Workflow4Metabolomics: A collaborative research infrastructure for computational metabolomics**. *Bioinformatics* doi:10.1093/bioinformatics/btu813

Help and support: [support@workflow4metabolomics.org](mailto:support@workflow4metabolomics.org)

Latest news

- 10/05/2017 - LC-MS: A new tutorial video explain **how to** run xcmsSet in parallel on single files [\[link\]](#)
- 20/04/2017 - Workflow4Metabolomics v3.0 starts today - Check the changelog section below

Changelog

Tutorials

LC/MS

MS

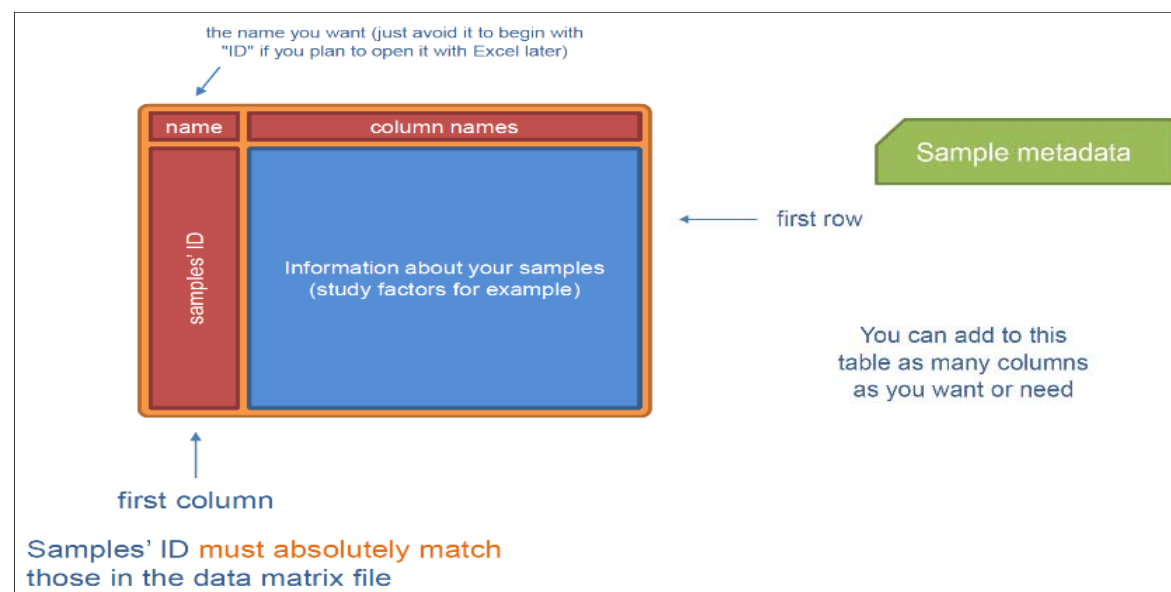
Common

History

search datasets

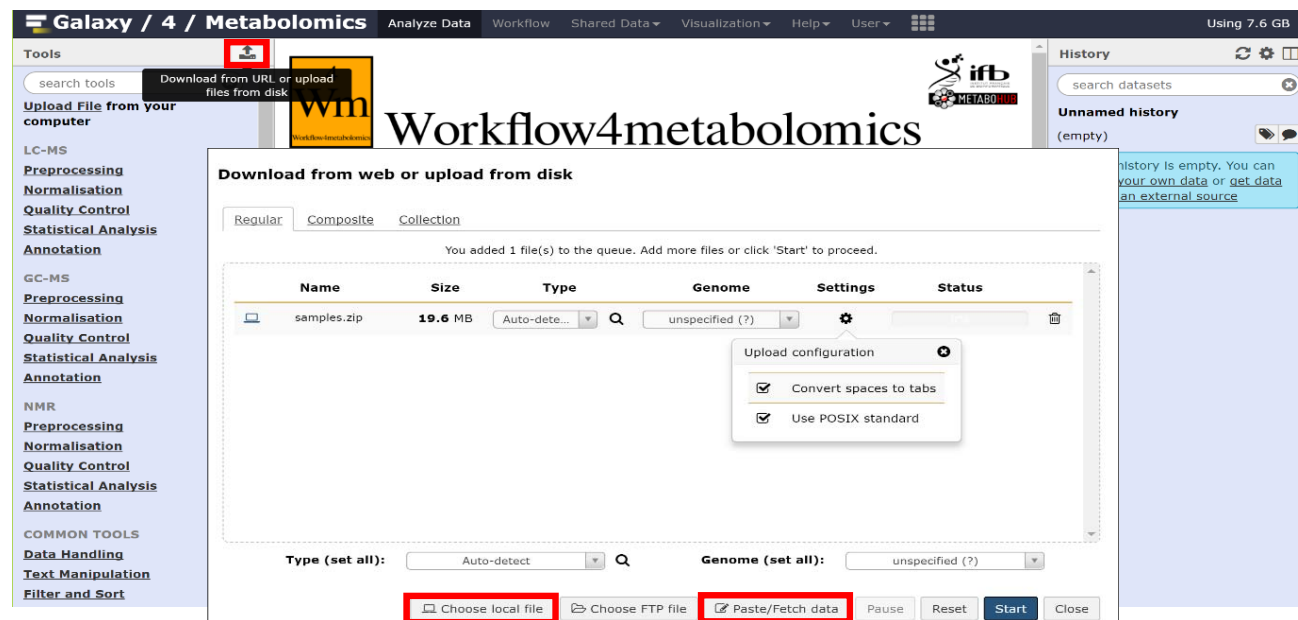
Unnamed history (empty)

This history is empty. You can [load your own data](#) or [get data from an external source](#)



# SESIÓN PRÁCTICA. VISUALS\_5

sampleName	class	polarity	sampleType	batch	injectionOrder	diet
QC	one	positive	pool	B1	1	NA
C1	one	positive	sample	B1	7	C
HC3	one	positive	sample	B1	10	HC
BL	one	positive	blank	B1	12	NA
...	...	...	...	...	...	...



Galaxy / 4 / Metabolomics

Analyze Data Workflow Shared Data Visualization Help User Using 7.6 GB

Tools

Download from URL or upload files from disk

Upload File from your computer

LC-MS

Preprocessing  
Normalisation  
Quality Control  
Statistical Analysis  
Annotation

GC-MS

Preprocessing  
Normalisation  
Quality Control  
Statistical Analysis  
Annotation

NMR

Preprocessing  
Normalisation  
Quality Control  
Statistical Analysis  
Annotation

COMMON TOOLS




Data Handling  
Text Manipulation  
Filter and Sort

Workflow4metabolomics

Download from web or upload from disk

Regular Composite Collection




You added 1 file(s) to the queue. Add more files or click 'Start' to proceed.

Name	Size	Type	Genome	Settings	Status
 samples.zip	19.6 MB	Auto-dete...	unspecified (?)		

Upload configuration

- Convert spaces to tabs
- Use POSIX standard

Type (set all): Auto-detect Q Genome (set all): unspecified (?)

 Choose local file  Choose FTP file  Paste/Fetch data Pause Reset Start Close

History


search datasets

Unnamed history (empty)

history is empty. You can your own data or get data an external source

# SESIÓN PRÁCTICA. VISUALS\_6

Galaxy / 4 / Metabolomics Analyze Data Workflow Shared Data Visualization Help User Using 7.6 GB

Tools  Download from URL or upload files from disk

Upload File from your computer

LC-MS

Preprocessing  
 Normalisation  
 Quality Control  
 Statistical Analysis  
 Annotation

GC-MS

Preprocessing  
 Normalisation  
 Quality Control  
 Statistical Analysis  
 Annotation

NMR

Preprocessing  
 Normalisation  
 Quality Control  
 Statistical Analysis  
 Annotation

COMMON

Data Handling  
 Text Manipulation  
 Filtering

Workflow4metabolomics

History search datasets Unnamed history (empty)

Download from web or upload from disk

Regular Composite Collection

FTP files

This Galaxy server allows you to upload files via FTP. To upload some files, log in to the FTP server at <ftp.workflow4metabolomics.org> using your Galaxy credentials (email address and password).

Your FTP directory does not contain any files.

local file **Choose FTP file** Paste/Fetch data Pause Reset Start Close

Open Connection

Server: ftp.workflow4metabolomics.org Port: 21

URL: ftp://(username@)ftp.workflow4metabolomics.org/

Username: icorguile

Password: \*\*\*\*\*

Anonymous Login  Save Password

Connect Cancel

0 Bookmarks

Unsecured FTP connection

Unsecured FTP connection

Haslo will be sent in plaintext. Please contact your web hosting service provider for assistance.

Continue

Disconnect

Don't show again

Pomoc

samples.zip

12.3 MiB (12,845,056 bytes) z 19.6 MiB (62%, 1.6 MB/sec, Pozostalo sekund: 5)

Wysyłanie samples.zip

# SESIÓN PRÁCTICA. VISUALS\_7

**Download from web or upload from disk**

Regular Composite Collection

You added 1 file(s) to the queue. Add more files or click 'Start' to proceed.

Name	Size	Type	Genome	Settings	Status
samples.zip	19.6 MB				

FTP files

This Galaxy server allows you to upload files via FTP. To upload some files, log in to the FTP server at **ftp.workflow4metabolomics.org** using your Galaxy credentials (email address and password).

Available files: 1 files 19.6 MB

Name	Size	Created
samples.zip	19.6 MB	11/22/2017 05:09:03 PM

Type (set all): unspecified (?)

Choose local file Choose FTP file Paste/Fetch data Pause Reset **Start** Close

**Download from web or upload from disk**

Regular Composite Collection

Name	Size	Type	Genome	Settings	Status
LC_Positive_mzXML.zip	3.6 GB	Auto-dete...	unspecified (?)		100% ✓

Type (set all): Auto-detect Genome (set all): unspecified (?)

Choose local file Choose FTP file Paste/Fetch data Pause Reset Start **Close**

# SESIÓN PRÁCTICA. VISUALS\_8

**Galaxy / 4 / Metabolomics** Analyze Data Workflow Shared Data Visualization Help User Using 12.0 GB

**Workflow4metabolomics**

**Current version : 3.0**

**Publication:** Franck Giacconi, Gildas Le Corguillé, Mishari Monsoor, Marlon Landi, Pierre Pericard, Mélanie Pétéra, Christophe Duperier, Marie Tremblay-Franco, Jean-François Martin, Daniel Jacob, Sophie Goullitquer, Etienne A. Thévenot and Christophe Caron (2014). **Workflow4Metabolomics: A collaborative research infrastructure for computational metabolomics**. *Bioinformatics*. doi:10.1093/bioinformatics/btu813

**Help and support:** [support@workflow4metabolomics.org](mailto:support@workflow4metabolomics.org)

**Latest news**

- 10/05/2017 - LC-MS: A new tutorial video explain [how to run xcms](#) ([link](#))
- 20/04/2017 - Workflow4Metabolomics v3.0 starts today - [Check it](#)

**Changelog**

- 3.0.0 - 20/04/2017
  - LC-MS
    - Preprocessing
      - UPGRADE - xcms.\* (2.1.0): upgrade the 1.44.0 to 1.46.0
      - NEW** - xcms.\* (2.1.0): The W4M tools v take as input a single file. It will allow to several files and merge them afterward

**Upload File**

**Dataset Information**

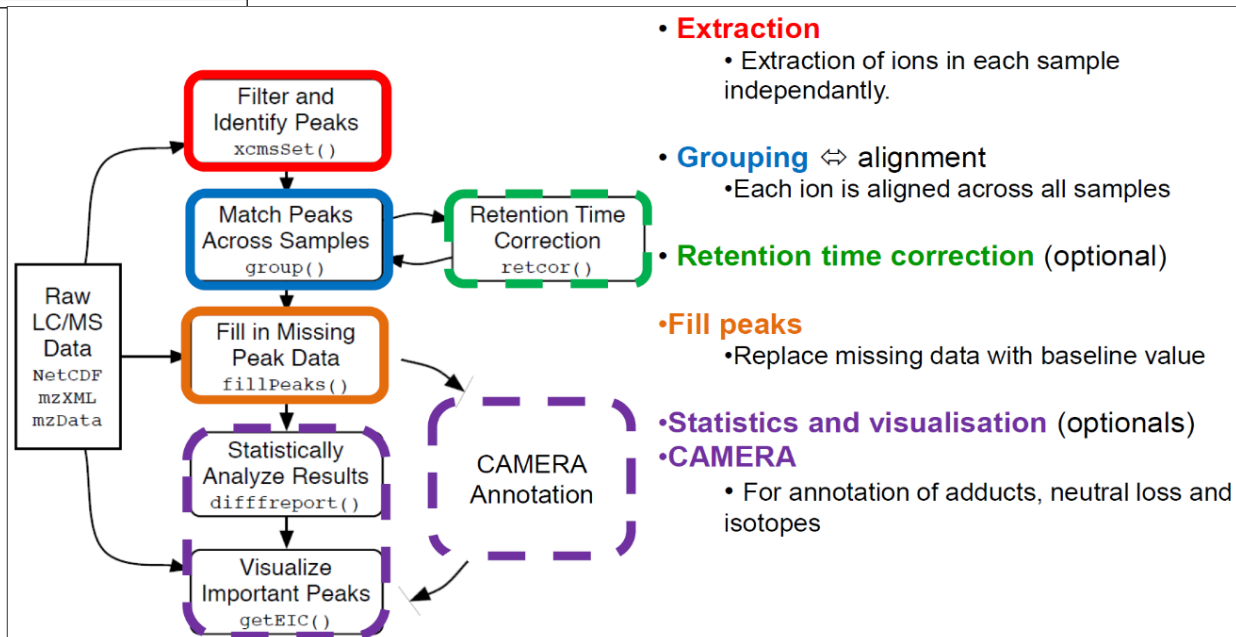
Number:	1
Name:	LC_Positive_mzXML.dp
Created:	Fri 24 Nov 2017 12:19:10 AM (UTC)
Filename:	0 bytes
DSkey:	?
Format:	txt

**Job Information**

Galaxy tool ID:	uploaded1
Galaxy Tool Version:	1.1.4
Tool Version:	
Tool Standard Output:	stdout
Tool Standard Error:	stderr
Tool Exit Code:	0
History Content API ID:	8d399c9b131f13b23
Job API ID:	c97c514f0105c63e
History API ID:	4e4095c119339f69
UUID:	9194cc24-ac90-410a-810c-410c79b5534

**Tool Parameters**

Input Parameter	Value	Note for rerun
file format:	auto	
async datasets:	None	
Specify Files for Dataset (auto):	1 uploaded datasets	
Genome:	unspecified (?)	
File Format:	auto	





# SESIÓN PRÁCTICA. VISUALS\_9

Galaxy / 4 / Metabolomics Analyze Data Workflow Shared Data Visualization Help User Using 15.6 GB

Tools

search tools

Upload File from your computer

LC-MS

Preprocessing

xcms.xcmsSet Filtration and Peak Identification using xcmsSet function from xcms R package to preprocess LC/MS data for relative quantification and statistical analysis

xcms.xcmsSet Merger Merge xcms.xcmsSet xset in one to be used by group

xcms.group Group peaks together across samples using overlapping m/z bins and calculation of smoothed peak distributions in chromatographic time.

xcms.retcor Retention Time Correction using retcor function from xcms R package

xcms.fillPeaks Integrate a sample's signal in regions where peak groups are not represented to create new peaks in missing areas

xcms.summary Create a

1 job has been successfully added to the queue - resulting in the following datasets:

- 1: LC\_Positive\_mzXML.L.zip
- 2: LC\_Positive\_mzXML.xset.RData
- 3: LC\_Positive\_mzXML.sampleMetadata.tsv
- 4: LC\_Positive\_mzXML.xset.TICs\_raw.pdf
- 5: LC\_Positive\_mzXML.xset.BPCs\_raw.pdf
- 6: LC\_Positive\_mzXML.xset.log.txt

You can check the status of queued jobs and view the resulting data by refreshing the History pane. When the job has been run the status will change from 'running' to 'finished' if completed successfully or 'error' if problems were encountered.

History

search datasets

Unnamed history

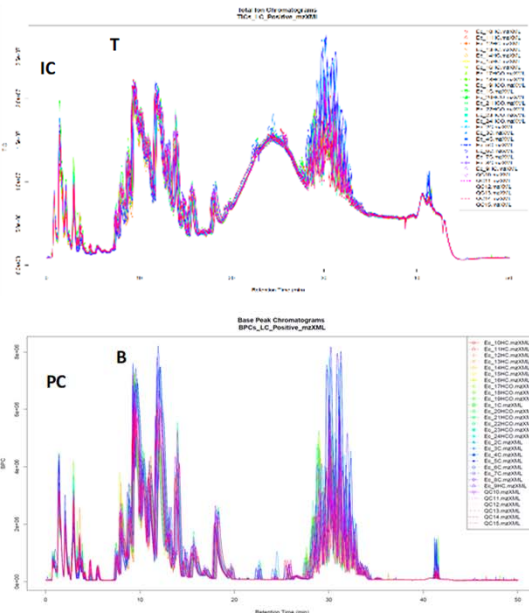
6 shown

3.61 GB

- 6: LC\_Positive\_mzXML.xset.log.txt
- 5: LC\_Positive\_mzXML.xset.BPCs\_raw.pdf
- 4: LC\_Positive\_mzXML.xset.TICs\_raw.pdf
- 3: LC\_Positive\_mzXML.sampleMetadata.tsv
- 2: LC\_Positive\_mzXML.xset.RData
- 1: LC\_Positive\_mzXML.L.zip

sample

1	Metadata	3
sampleMetadata	class	polarity
Ec_10HC	LC_Positive_mzXML	positive
Ec_11HC	LC_Positive_mzXML	positive
Ec_12HC	LC_Positive_mzXML	positive
Ec_13HC	LC_Positive_mzXML	positive
Ec_14HC	LC_Positive_mzXML	positive
Ec_15HC	LC_Positive_mzXML	positive
Ec_16HC	LC_Positive_mzXML	positive
Ec_17HCO	LC_Positive_mzXML	positive
Ec_18HCO	LC_Positive_mzXML	positive
Ec_19HCO	LC_Positive_mzXML	positive
Ec_1C	LC_Positive_mzXML	positive
Ec_20HCO	LC_Positive_mzXML	positive
Ec_21HCO	LC_Positive_mzXML	positive
Ec_22HCO	LC_Positive_mzXML	positive
Ec_23HCO	LC_Positive_mzXML	positive
Ec_24HCO	LC_Positive_mzXML	positive
Ec_2C	LC_Positive_mzXML	positive
Ec_3C	LC_Positive_mzXML	positive
Ec_4C	LC_Positive_mzXML	positive
Ec_5C	LC_Positive_mzXML	positive
Ec_6C	LC_Positive_mzXML	positive
Ec_7C	LC_Positive_mzXML	positive
Ec_8C	LC_Positive_mzXML	positive
Ec_9HC	LC_Positive_mzXML	positive
QC10	LC_Positive_mzXML	positive
QC11	LC_Positive_mzXML	positive
QC12	LC_Positive_mzXML	positive
QC13	LC_Positive_mzXML	positive
QC14	LC_Positive_mzXML	positive
QC15	LC_Positive_mzXML	positive



info

Data processing

PACKAGE INFO

```
parallel 3.2.5
BioGenerics 0.18.1
Biobase 2.30.0
Rcpp 0.12.10
RGR 2.4.1
rjson 1.0.0.0
time 0.4.2
tween 1.1.4
```

ARGUMENTS INFO

```
zipfile /usr/local/project/edu/galaxy/metabolomics/galaxy-dist/database/files/000/439/dataset_439795.dat
xfunction xcmsSet
xsetDataOutput /usr/local/project/edu/galaxy/metabolomics/galaxy-dist/database/files/000/440/dataset_440044.dat
xsampleMetadata /usr/local/project/edu/galaxy/metabolomics/galaxy-dist/database/files/000/440/dataset_440044.dat
tlicpdf /usr/local/project/edu/galaxy/metabolomics/galaxy-dist/database/files/000/440/dataset_440046.dat
tlicpdf /usr/local/project/edu/galaxy/metabolomics/galaxy-dist/database/files/000/440/dataset_440047.dat
nSlaves 4
method centroid
ppm 25
width 1 (-3x, 6x)
widthF 0.0015
subsearch 10
integrate 1
noise 0
prefilter (-), 1000
```

INFIL PROCESSING INFO

ARGUMENTS PROCESSING INFO

```
files_root_directory LC_Positive_mzXML
Compute m/z checksum...
Checking file structure...
Checking files filenames compatibility with mcs...
```

# SESIÓN PRÁCTICA. VISUALS\_10

`xcms.group` Group peaks together across samples using overlapping m/z bins and calculation of smoothed peak distributions in chromatographic time.

		pool1B1			pool1B2			pool1B3		
		mz	rt	int	mz	rt	int	mz	rt	int
Listas de picos independientes		196.0905	66.6	7810936	196.0910	66.7	11733921	196.0902	66.6	7933325
		158.1180	67.4	71736	342.0310	69.0	74594	158.1173	67.4	82969
		342.0308	67.6	202268	267.0581	65.5	260877	342.0308	21.3	2581
		267.0581	65.5	282039	283.0318	65.2	424631	283.0320	65.3	357448
Iones del grupo por m/z		196.0905	66.6	7810936	196.0910	66.7	11733921	196.0902	66.6	7933325
		158.1180	67.4	71736	342.0310	69.0	74594	158.1173	67.4	82969
		342.0308	67.6	202268	267.0581	65.5	260877	342.0308	21.3	2581
		267.0581	65.5	282039	283.0318	65.2	424631	283.0320	65.3	357448
Iones del grupo por RT		196.0905	66.6	7810936	196.0910	66.7	11733921	196.0902	66.6	7933325
		158.1180	67.4	71736				158.1173	67.4	82969
		342.0308	67.6	202268	342.0310	69.0	74594	342.0308	21.3	2581
		267.0581	65.5	282039	267.0581	65.5	260877			
<b>Matriz</b>										
	mz	rt	pool1B1	pool1B2	pool1B3					
	196.0905	66.6	7810936	11733921	7933325					
	158.1176	67.4	71736		82969					
	342.0308	21.3			2581					
	342.0309	68.3	202268	74594						
	267.0581	65.5	282039	260877						
	283.0319	65.2		424631	357448					

Parameter : num + label	Format
Or : RData file   rdata.xcms.raw	
Or : RData file   rdata.xcms.retcor	

# SESIÓN PRÁCTICA. VISUALS\_11

**xcms.group** Group peaks together across samples using overlapping m/z bins and calculation of smoothed peak distributions in chromatographic time. (Galaxy Version 2.1.0) Versions Options

**xset RData file**

No rdata.xcms.raw, rdata.xcms.group, rdata.xcms.retcor or rdata dataset available. ▼  
output file from another function xcms (xcmsSet, retcor etc.)

**Method to use for grouping**

density ▼  
[method] See the help section below

**Bandwidth**

30  
[bw] bandwidth (standard deviation or half width at half maximum) of gaussian smoothing kernel to apply to the peak density chromatogram

**Minimum fraction of samples necessary**

0.5  
[minfrac] in at least one of the sample groups for it to be a valid group

**Width of overlapping m/z slices**

0.01  
[mzwid] to use for creating peak density chromatograms and grouping peaks across samples

**Advanced options**

show ▼

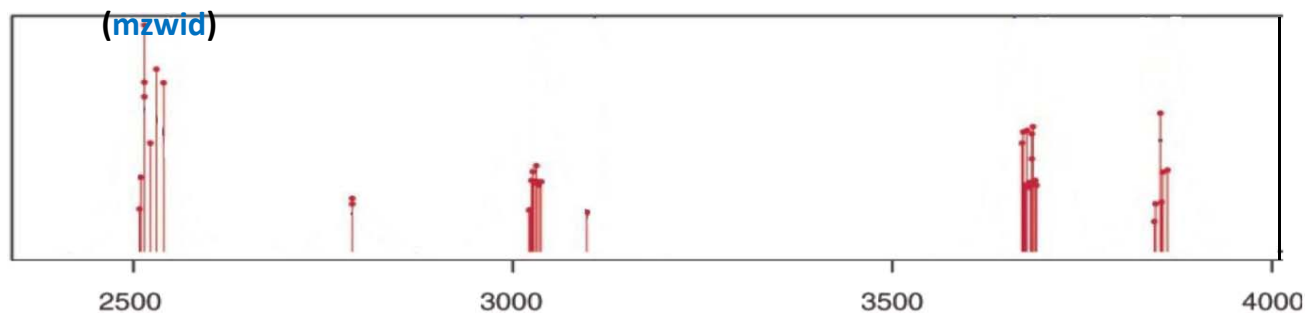
**Maximum number of groups to identify in a single m/z slice**

50  
[max]

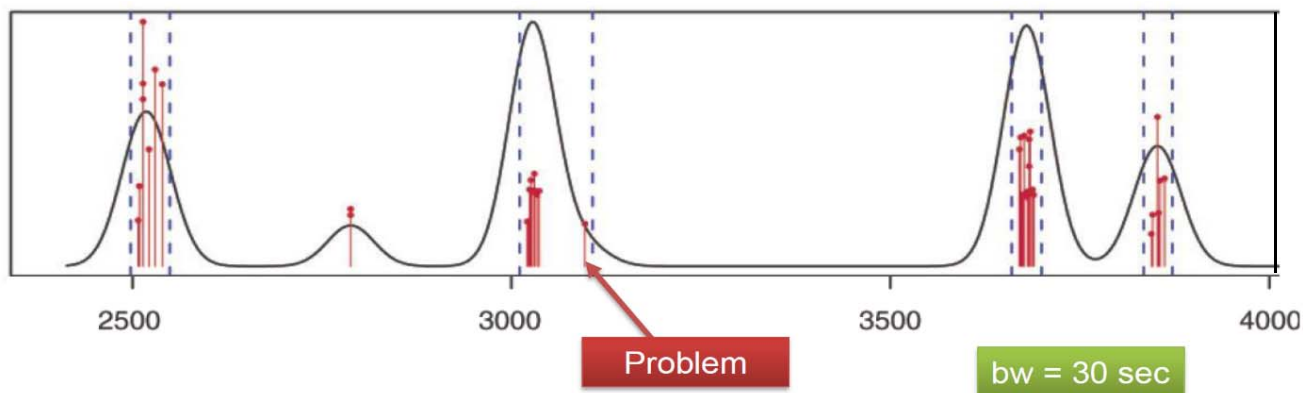
**Get a Peak List**

# SESIÓN PRÁCTICA. VISUALS\_12

Agrupación de picos en *bin* de masa: 337.975 – 338.225 m/z

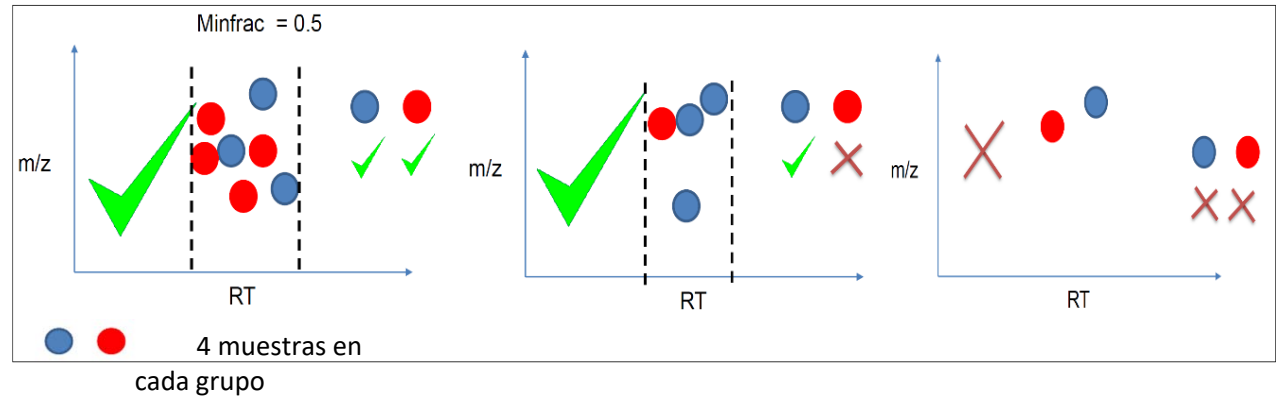
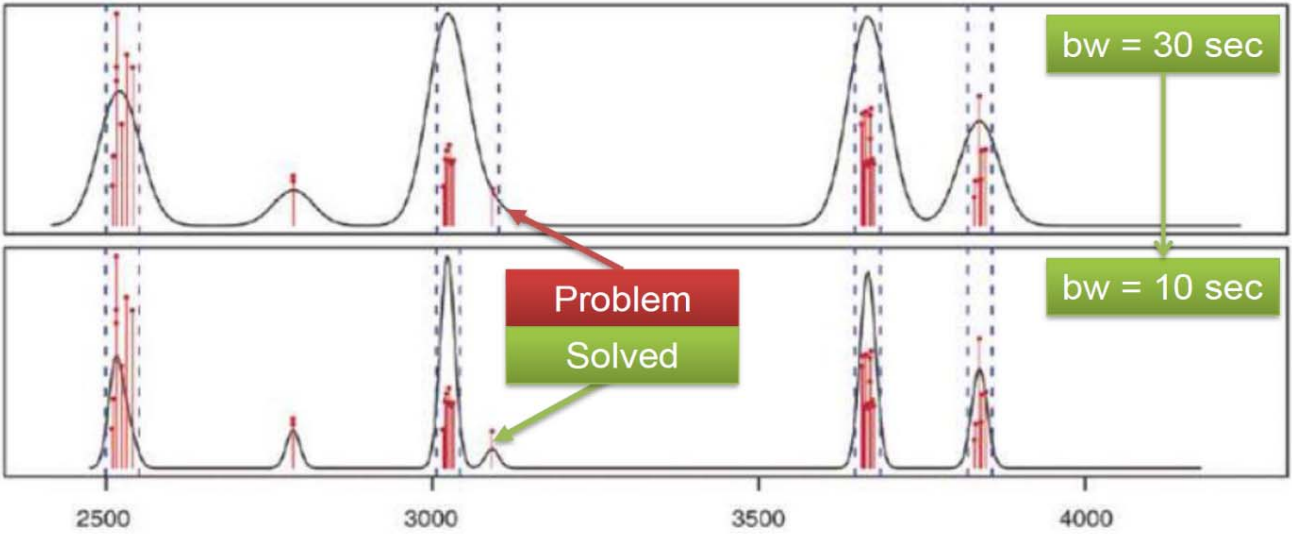


Agrupación de picos en *bin* de masa: 337.975 – 338.225 m/z (mzwid)



# SESIÓN PRÁCTICA. VISUALS\_13

Agrupación de picos en bin de masa: 337.975 – 338.225 m/z (mzwid)









# SESIÓN PRÁCTICA. VISUALS\_15

[xcms.retcor](#) Retention Time Correction using retcor function from xcms R package

Parameter : num + label	Format
1 : RData file	rdata.xcms.group

**xcms.retcor Retention Time Correction using retcor function from xcms R package (Galaxy Version 2.1.0)**

 Versions
 
 Options

**xset RData file**

📄 📁 📂

output file from another function xcms (xcmsSet, retcor etc.)

**Method to use for retention time correction**

[method] See the help section below

**Smooth method**

[smooth] either 'loess' for non-linear alignment or 'linear' for linear alignment


**Number of extra peaks to allow in retention time correction correction groups**

[extra]

**Number of missing samples to allow in retention time correction groups**

[missing] Number of admitted missing well behaved peak in a group.

**Advanced options**

**Resubmit your raw dataset or your zip file** 

✓ Execute

# SESIÓN PRÁCTICA. VISUALS\_16

## Advanced options

show ▼

### Degree of smoothing for local polynomial regression fitting

0.2

[span]

### Family

gaussian ▼

[family] if gaussian fitting is by least-squares with no outlier removal, and if symmetric a re descending M estimator is used with Tukey's biweight function, allowing outlier removal

### plottype

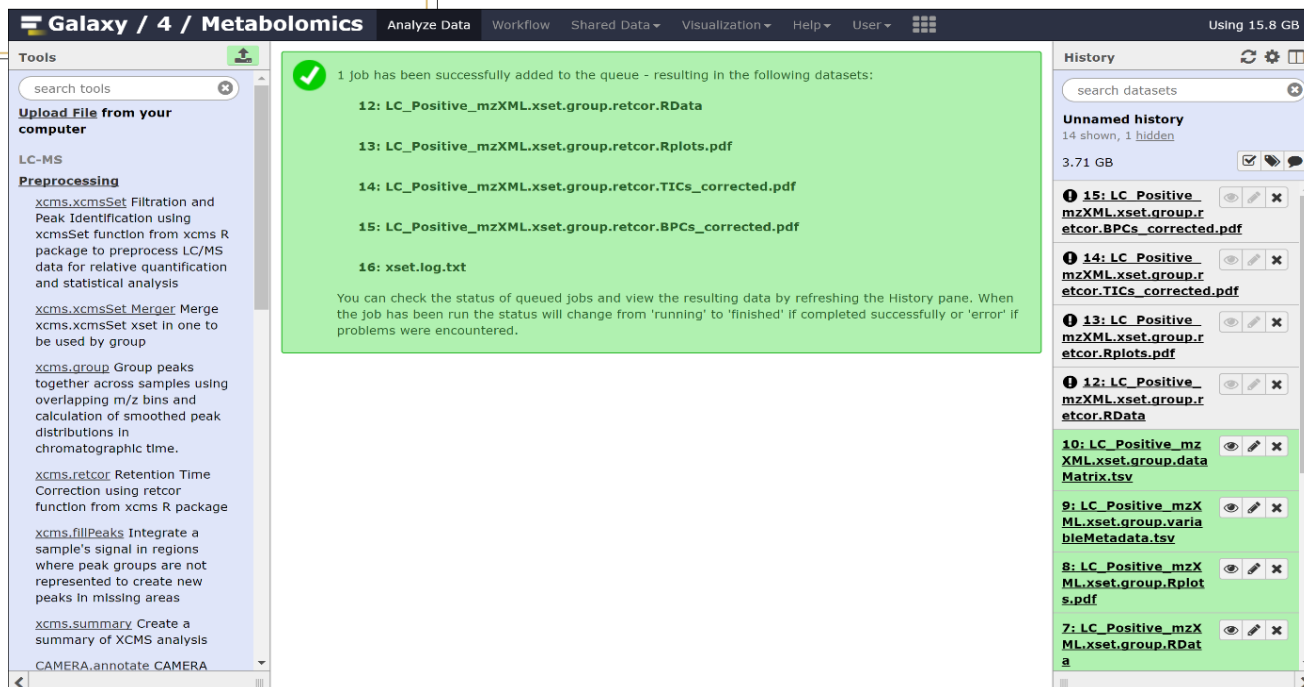
deviation ▼

**Plot to visualize the result of the retention time correction.**

[plottype] if deviation plot retention time deviation points and regression fit, and if mdevden also plot peak overall peak density and retention time correction peak density

**Resubmit your raw dataset or your zip file** 

 **Execute**



**Galaxy / 4 / Metabolomics** Analyze Data Workflow Shared Data Visualization Help User Using 15.8 GB

**Tools**

search tools

**Upload File from your computer**

LC-MS

**Preprocessing**

- [xcms.xcmsSet](#) Filtration and Peak Identification using xcmsSet function from xcms R package to preprocess LC/MS data for relative quantification and statistical analysis
- [xcms.xcmsSet Merger](#) Merge xcms.xcmsSet xset in one to be used by group
- [xcms.group](#) Group peaks together across samples using overlapping m/z bins and calculation of smoothed peak distributions in chromatographic time.
- [xcms.retcor](#) Retention Time Correction using retcor function from xcms R package
- [xcms.fillPeaks](#) Integrate a sample's signal in regions where peak groups are not represented to create new peaks in missing areas
- [xcms.summary](#) Create a summary of XCMS analysis
- [CAMERA.annotate](#) CAMERA

**History**

search datasets

**Unnamed history**  
14 shown, 1 hidden  
3.71 GB

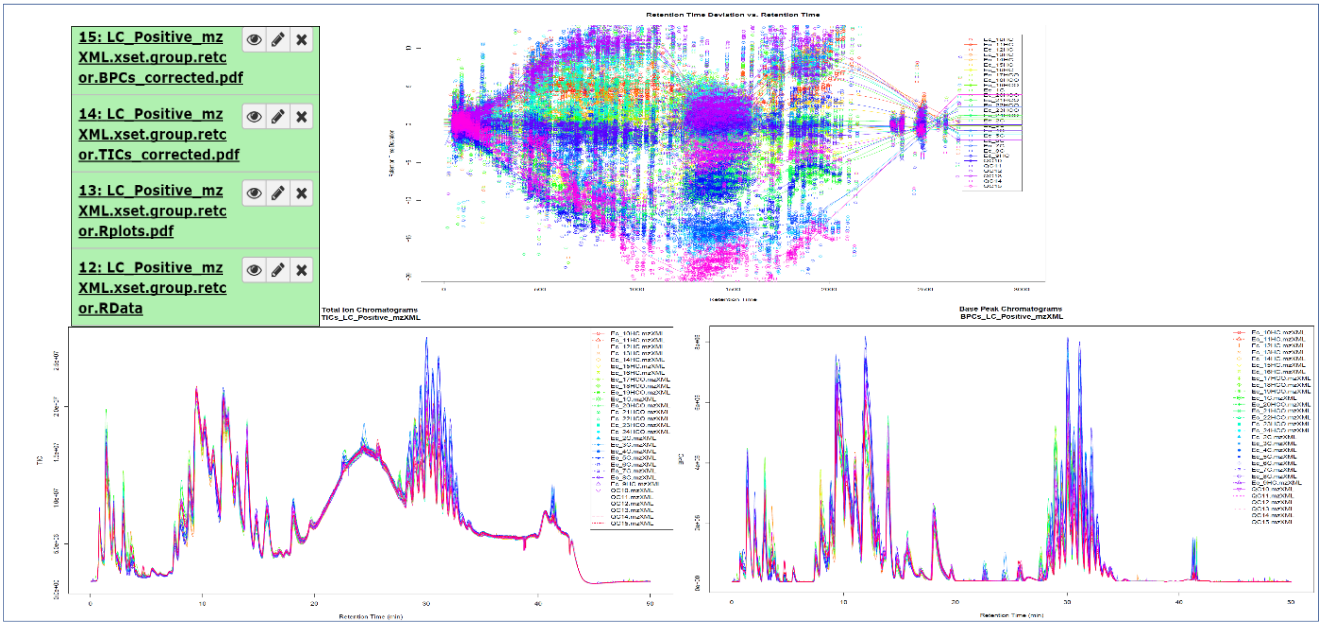
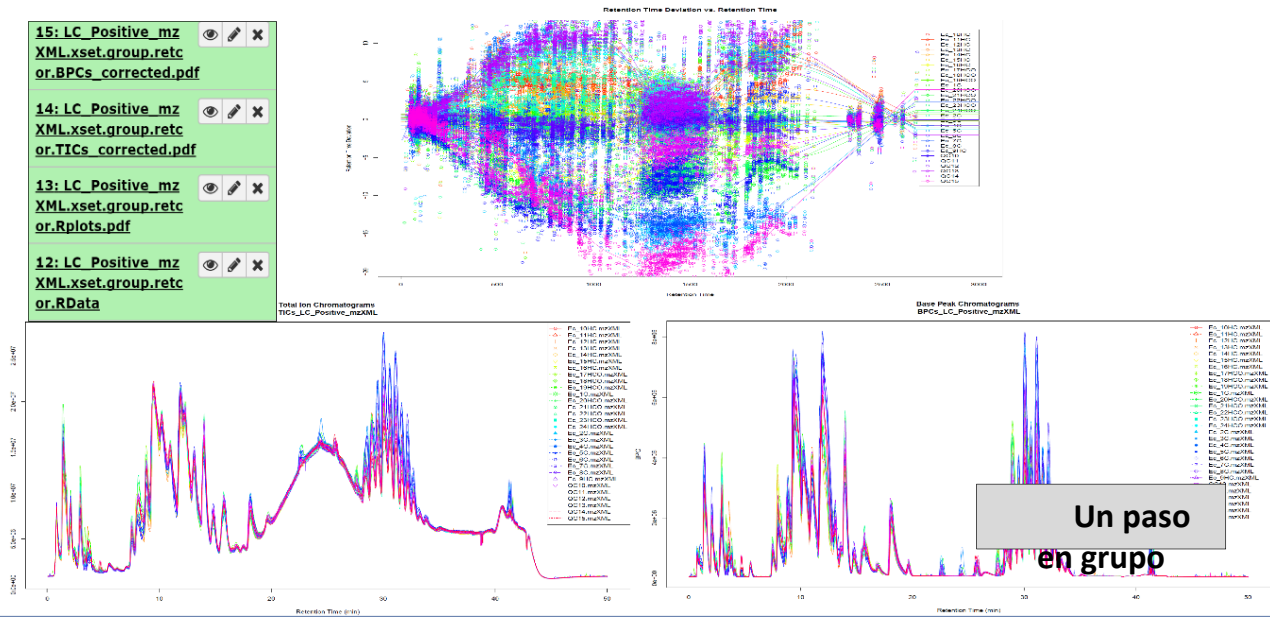
- 15: LC\_Positive\_mzXML.xset.group.retcor.BPCs\_corrected.pdf
- 14: LC\_Positive\_mzXML.xset.group.retcor.TICs\_corrected.pdf
- 13: LC\_Positive\_mzXML.xset.group.retcor.Rplots.pdf
- 12: LC\_Positive\_mzXML.xset.group.retcor.RData
- 10: LC\_Positive\_mzXML.xset.group.data.Matrix.tsv
- 9: LC\_Positive\_mzXML.xset.group.varia.bleMetadata.tsv
- 8: LC\_Positive\_mzXML.xset.group.Rplots.pdf
- 7: LC\_Positive\_mzXML.xset.group.RData

**Message:** 1 job has been successfully added to the queue - resulting in the following datasets:

- 12: LC\_Positive\_mzXML.xset.group.retcor.RData
- 13: LC\_Positive\_mzXML.xset.group.retcor.Rplots.pdf
- 14: LC\_Positive\_mzXML.xset.group.retcor.TICs\_corrected.pdf
- 15: LC\_Positive\_mzXML.xset.group.retcor.BPCs\_corrected.pdf
- 16: xset.log.txt

You can check the status of queued jobs and view the resulting data by refreshing the History pane. When the job has been run the status will change from 'running' to 'finished' if completed successfully or 'error' if problems were encountered.

# SESIÓN PRÁCTICA. VISUALS\_17



# SESIÓN PRÁCTICA. VISUALS\_18

Galaxy / 4 / Metabolomics Analyze Data Workflow Shared Data Visualization Help User Using 15.8 GB

Tools

search tools

xcmsSet function from xcms R package to preprocess LC/MS data for relative quantification and statistical analysis

xcms.xcmsSet Merger Merge xcms.xcmsSet xset in one to be used by group

xcms.group Group peaks together across samples using overlapping m/z bins and calculation of smoothed peak distributions in chromatographic time.

xcms.retcor Retention Time Correction using retcor function from xcms R package

xcms.fillPeaks Integrate a sample's signal in regions where peak groups are not represented to create new peaks in missing areas

xcms.summary Create a summary of XCMS analysis

CAMERA.annotate CAMERA annotate function. Returns annotation results (isotope peaks, adducts and fragments) and a diffreport if more than one condition.

CAMERA.comblnxsAnnos Wrapper function for the

1 job has been successfully added to the queue - resulting in the following datasets:

- 17: LC\_Positive\_mzXML.xset.group.retcor.group.RData
- 18: LC\_Positive\_mzXML.xset.group.retcor.group.Rplots.pdf
- 19: LC\_Positive\_mzXML.xset.group.retcor.group.variableMetadata.tsv
- 20: LC\_Positive\_mzXML.xset.group.retcor.group.dataMatrix.tsv
- 21: xset.log.txt

You can check the status of queued jobs and view the resulting data by refreshing the History pane. When the job has been run the status will change from 'running' to 'finished' if completed successfully or 'error' if problems were encountered.

History

search datasets

Unnamed history  
18 shown, 2 hidden  
3.73 GB

- 20: LC\_Positive\_mzXML.xset.group.retcor.group.dataMatrix.tsv
- 19: LC\_Positive\_mzXML.xset.group.retcor.group.variableMetadata.tsv
- 18: LC\_Positive\_mzXML.xset.group.retcor.group.Rplots.pdf
- 17: LC\_Positive\_mzXML.xset.group.retcor.group.RData
- 15: LC\_Positive\_mzXML.xset.group.retcor.group.BPCs\_corrected.pdf
- 14: LC\_Positive\_mzXML.xset.group.retcor.group.TICs\_corrected.pdf
- 13: LC\_Positive\_mzXML.xset.group.retcor.group.Rplots.pdf
- 12: LC\_Positive\_mzXML.xset.group.retcor.group.RData

Un paso en grupo

**xcms.fillPeaks** Integrate a sample's signal in regions where peak groups are not represented to create new peaks in missing areas

Parameter : num + label	Format
1 : RData file	rdata.xcms.group

**xcms.fillPeaks** Integrate a sample's signal in regions where peak groups are not represented to create new peaks in missing areas (Galaxy Version 2.1.0)

Versions Options

**xset RData file**

output file from another xcms function (group)

**Filling method**

[method] See the help section below

**Get a Peak List**

**Resubmit your raw dataset or your zip file**

# SESIÓN PRÁCTICA. VISUALS\_19

**Galaxy / 4 / Metabolomics** Analyze Data Workflow Shared Data Visualization Help User Using 15.9 GB

**Tools**

- search tools
- xcms.xcmsSetSummary Summary function from xcms R package to preprocess LC/MS data for relative quantification and statistical analysis
- xcms.xcmsSetMerger Merge xcms.xcmsSet in one to be used by group
- xcms.group Group peaks together across samples using overlapping m/z bins and calculation of smoothed peak distributions in chromatographic time.
- xcms.retcor Retention Time Correction using retcor function from xcms R package
- xcms.fillPeaks Integrate a sample's signal in regions where peak groups are not represented to create new peaks in missing areas
- xcms.summary Create a summary of XCMS analysis
- CAMERA.annotate CAMERA annotate function. Returns annotation results (isotope peaks, adducts and fragments) and a diffplot if more than one condition.
- CAMERA.combineXenonAnno wrapper function for the

**History** search datasets 3.82 GB

21 shown, 3 hidden

- 24: LC\_Positive\_mzXML.xset.group.retcor.group.fillPeaks.dataMatrix.tsv
- 23: LC\_Positive\_mzXML.xset.group.retcor.group.fillpeaks.variableMetadata.tsv
- 22: LC\_Positive\_mzXML.xset.group.retcor.group.fillpeaks.dataMatrix.tsv
- 20: LC\_Positive\_mzXML.xset.group.retcor.group.dataMatrix.tsv
- 19: LC\_Positive\_mzXML.xset.group.retcor.group.variableMetadata.tsv
- 18: LC\_Positive\_mzXML.xset.group.retcor.group.Rplots.pdf
- 17: LC\_Positive\_mzXML.xset.group.retcor.group.RData
- 15: LC\_Positive\_mzXML.xset.group.retcor.group.RData

1 job has been successfully added to the queue - resulting in the following datasets:

- 22: LC\_Positive\_mzXML.xset.group.retcor.group.fillPeaks.RData
- 23: LC\_Positive\_mzXML.xset.group.retcor.group.fillpeaks.variableMetadata.tsv
- 24: LC\_Positive\_mzXML.xset.group.retcor.group.fillpeaks.dataMatrix.tsv
- 25: xset.log.txt

You can check the status of queued jobs and view the resulting data by refreshing the History pane. When the job has been run the status will change from "running" to "finished" if completed successfully or "error" if problems were encountered.

variableMeta					dataM				
data.tsv					atrix.tsv				
1	2	3	4	5	1	2	3	4	5
name	namecustom	mz	mzmin	mzmax	name	Ec_10HC	Ec_11HC	Ec_12HC	Ec_13HC
M103T2673	M102.9703T44.55	102.970311351949	102.970195579109	102.970399312385	M103T2673	1061832.30493052	1144403.44135983	1020539.16801412	1121248.09306137
M104T52	M104.10770.86	104.106964995157	104.105982748003	104.107508430139	M104T52	116131.202463165	113145.345969103	221247.835289123	85812.9626298084
M107T56	M107.0706T0.94	107.070606586921	107.070137215825	107.071251918772	M107T56	11028.4704300842	24224.0223756465	40340.7417124155	20019.0940904541
M109T176	M109.10172.93	109.100995864082	109.100845900078	109.101142306016	M109T176	201788.89433418	208794.490735228	95350.587358747	100622.014506292
M110T66_1	M110.0712T1_1_1	110.071232504779	110.071135326801	110.071413890512	M110T66_1	447052.480245756	509069.134419706	529036.944020849	419073.389406295
M110T66_2	M110.1451T1.11_2	110.145035383832	110.144834345671	110.145230783207	M110T66_2	29398.8525611569	33127.152696311	36290.5541728252	27314.1463684311
M111T79	M111.1168T1.31	111.116790950832	111.116666786018	111.116966139657	M111T79	154633.650364231	107591.113126188	162187.205989563	153506.517209983
M111T180	M111.1165T3	111.116486144107	111.116213639299	111.11662410968	M111T180	54067.0514414524	65254.58342024	49274.2740727852	60560.6364823781
M112T51	M112.0521T0.86	112.052056215129	112.051444952237	112.052702344446	M112T51	82566.9537246094	100534.324090609	98626.7065472707	98909.7776453247
M112T79	M112.1201T1.31	112.120663107016	112.119644951814	112.120278047431	M112T79	12748.4660072896	20138.4564137684	13863.0038125153	12884.1150847926
M113T48	M112.8959T0.81	112.895923556653	112.895275075808	112.896851780014	M113T48	66262.9480098419	62663.7677114182	88327.424822492	70933.4877627869
M113T59	M112.9995T0.98	112.999451218223	112.999065891781	112.999691444871	M113T59	96435.8076669617	85020.2573272705	84614.7288627994	90950.2532185818
M115T48	M114.8933T0.81	114.893232974783	114.892556681008	114.894135034299	M115T48	32698.9970340881	32496.02112052232	41719.2826053286	31671.5001469726
M116T54	M116.0706T0.9	116.070621610785	116.07008824786	116.070868028302	M116T54	172069.77323927	199833.290424495	259939.762536967	189934.579256049
M117T171	M117.0697T2.85	117.069716380854	117.069232623419	117.070682716424	M117T171	25315.1286311528	28061.6590161876	17398.6140722212	19771.6361491645
M118T2331_1	M118.0862T38.85_1	118.086184577653	118.086051978809	118.08632326958	M118T2331_1	425563.804303394	338087.459169224	394919.650605011	266230.851963383
M118T53_1	M118.0860T70.88_1	118.086740230705	118.086065712653	118.08718457984	M118T53_1	14370174.3398173	11354958.4483364	13709306.7272189	8072194.34844452
M118T112	M118.0862T1.87	118.086184011752	118.086107212736	118.086292372487	M118T112	2716813.17062041	2023073.28526089	2918253.74628112	1559191.99272233
M118T2331_2	M118.1624T38.85_2	118.162424196361	118.162275890008	118.162654424063	M118T2331_2	29155.2018136445	20060.6112223546	25748.7617057155	14566.8909274575
M118T53_2	M118.1625T0.88_2	118.162541997427	118.161930061116	118.16295469244	M118T53_2	1645565.67086	1214220.15293176	1501034.72970629	818662.841329422
M118T52_1	M118.1887T0.87_1	118.187994739206	118.187269133652	118.188064468827	M118T52_1	146040.357902741	115410.21893396	147278.242704987	73784.7286913757
M118T52_2	M118.2124T0.87_2	118.212381136854	118.211443391281	118.212900282301	M118T52_2	143442.314667542	111096.156310303	143350.57062082	69977.2087654114
M118T52_3	M118.2365T0.87_3	118.236519662066	118.2358711863	118.237141740029	M118T52_3	1627977.36458696	78505.770380249	103179.631372188	48305.8035364075
M119T53_1	M119.0895T0.88_1	119.089482441589	119.08882743951	119.08995212236	M119T53_1	798878.512076424	636208.391813786	754206.198042717	451126.926595215
M119T2330	M119.0885T38.84	119.088498058298	119.088215220181	119.08889805151	M119T2330	24954.8740942383	23399.8112346703	23575.9488785678	13338.1884562498
M119T53_2	M119.1656T0.88_2	119.165632425698	119.164957479794	119.166194657233	M119T53_2	54103.2992341919	49257.9664361572	60770.7195596075	35086.4712632904
M121T173	M121.1002T2.88	121.1001599399284	121.100016017078	121.100255809592	M121T173	240164.240526719	3207661.5872076	331021.874998269	251582.171688811
M121T1739	M121.1001T28.98	121.100136272057	121.09952084354	121.100214241705	M121T1739	2425847.45517966	174789.838189487	288696.654292461	249404.370447165
M121T176	M121.1241T2.94	121.124074506687	121.123181163719	121.12682345796	M121T176	352694.554213724	130687.160363821	426307.452419805	24478.4578494873



# SESIÓN PRÁCTICA. VISUALS\_20

**24: LC\_Positive\_mz**

**XML.xset.group.ret**

**or.group.fillpeaks.dataMatrix.t**

**v**

6,929 lines

format: **tabular**, database: ?

**PACKAGE INFO**

parallel 3.2.5

BiocGenerics 0.16.1

Biobase 2.30.0

Rcpp 0.12.10

mzR 2.4.1

xcms 1.46.0

snow 0.4.2

batch 1.1.4

**ARGUMENTS INFO**

xfunction fillPeaks

Image

/work/project/w4m/galaxy4metab

dist/database/files/000/440/datas

### Matriz de datos exportada

name	Ec_10HC	Ec_11HC	Ec_12HC	Ec_13HC	Ec_14HC	Ec_15HC	Ec_16HC	Ec_17HCO	Ec_18HCO	Ec_19HCO	Ec_1C	Ec_20HCO	Ec_21HCO	Ec_22HCO	Ec_23HCO	Ec_24HCO	Ec_2C	Ec_3C	Ec_4	
1	M1037267	1061832	1144403	1202539	1212248	947508.3	1045868	978855.6	1175380	1011507	118730	1150975	975248.5	1031258	457588.8	878824.4	1019229	1088809	1136409	10
2	M104752	116131.2	113145.3	221247.8	85812.96	146116.3	140097.1	133505.4	86630.77	95829.4	96932.66	43766.73	109815.5	124091.2	102362.2	122175.4	132149.1	47053.63	59721.62	463
3	M107756	11028.47	24224.02	40340.74	20019.09	26727.98	19011.27	35323.02	20886.77	18390.19	23702.54	23869.28	23943.1	24901.63	19243.22	16770.16	24718.96	20585.67	28613.4	201
4	M109176	201788.9	208794.5	95350.59	100622	194415.7	127442.4	113288.2	196363.7	389619.8	217344	237685.2	218852.2	272707.9	151016.4	133146.2	114873.2	148750.3	218011.8	133
5	M110766	44705.25	509699.1	529036.9	419073.4	412756.3	529367.8	391197.7	538527.8	543039.3	532286.6	672981.9	460273.1	529586.6	399481.3	534636.6	511456.8	636621.1	564149.4	562
6	M110766	29398.85	33212.15	36290.55	27214.15	27749.53	34127.79	25516.78	34531.99	31252.68	35446.52	45575.19	33088.11	37144.59	21891.53	36946.01	33620.55	41071.43	353151.01	385
7	M111179	154633.7	107591.1	162187.2	153509.5	169885.5	112960.5	157391.6	105751.8	86714.63	98921.62	115968.6	238308.7	153576.9	92006.39	126529	159932.3	111906.3	99650.9	104
8	M111180	54067.05	65254.58	49274.27	60560.64	56842.71	79019.7	65522.75	61210.14	110854.6	67253.51	64479.75	63502.71	84569.38	92845.65	83259	62958.21	69265.39	5379.49	573
9	M112751	82566.95	100534.3	98626.71	89809.78	99830.09	107412.1	93364.82	94608.51	89708.21	82677.17	77575.35	102612.2	108832.4	89941.34	93667.31	103061.6	96405.49	77078.09	911
10	M112779	12748.47	20138.46	13869	12884.12	12731.65	21747.13	13215.56	20259.91	17220.5	21101.15	18760.8	23401.64	12511.27	16114.86	10182.54	12618.25	18439.15	14202.86	195
11	M113148	66262.95	62663.77	88327.42	70933.49	68463.19	81837.4	88823.26	52497.03	67809.3	34205.02	49157.28	86037.92	62005.08	42987.11	69887.25	61477.21	38803.76	41662.85	281
12	M113159	96435.81	85020.26	84614.73	96950.25	83132.07	89945.89	87088.7	109169.2	90344.09	101318.5	152500.6	105461	92616.84	94935.86	70281.61	79582.32	152045.6	162440.9	134
13	M115148	32091	32496.02	41719.28	31671.5	32969.86	44350.62	44357.66	25932.56	15777.95	11776.8	26325.72	48005.22	33828.57	28310.83	34330.24	31391.11	18951.08	21805.35	273
14	M116754	172069.8	199833.3	259939.8	189934.6	195105.2	239906.9	205441.7	180374.6	176592.2	200264.9	169972.1	204549.7	175611.2	165365.3	202068.1	213644.5	22074.8	192031.8	166
15	M1177171	25315.13	28091.66	17398.61	19771.64	14305.55	30913.3	17978.14	25773.44	31245.05	25222.35	38144.71	22604.85	30235.47	22155.06	31155.07	28308.49	33011.4	38659.66	275
16	M118233	425563.8	338087.5	394919.7	266230.9	526366.9	363375.3	248248	280576.4	207221.9	288967.7	251278.5	288688.1	372121.4	323816.9	291506.3	368688	226753.5	305659.1	291
17	M118753	14370174	11354958	13709307	8072194	15334177	11814324	8434178	7379334	7208947	7454897	3643826	12433611	11406345	9192595	10015179	13592387	7736001	7611000	68
18	M1187112	2716813	2033073	2918254	1559192	2833037	2127166	1465745	1365296	1137802	1287075	713326.2	2185308	184210	162428	1540899	2958062	9288389	1066894	982
19	M1187233	29155.2	206060.61	25748.76	14566.89	34234.07	23916.89	16655	17578.42	10762.96	15281.99	19255.18	24177.14	18135.73	17026.41	21657.19	15197.02	17589.02	165	
20	M118753	1645566	1214220	1501035	818662.8	1754264	1246622	887988.6	739222	71981.1	745133.8	435892.3	1356507	1263127	1115128	932822.4	1522090	782386.9	751276.9	711
21	M118752	146404.0	115410.2	147278.2	73784.73	180394.3	117377.9	84299.53	66006.05	61898.48	73686.84	25228.96	1533264	124390.7	106251.7	89433.6	152055.6	781939.4	50443.41	665
22	M118752	143442.3	111096.2	143350.6	69977.21	177728.3	112887.7	80537	63235.3	59029.35	69600.07	22661.69	1353264	121611.4	100314.3	84359.51	150006.2	775875.7	49053.04	627
23	M118752	1627977	78505.77	103179.6	48305.8	131062.6	80797.53	54655.8	44279.75	39887.74	45365.3	23545.19	1344630	87993.92	72424.75	59866.54	108794.5	778445.6	34642.17	436
24	M119753	798878.5	636208.4	754206.2	451126.9	833842.5	660059.2	477399.7	417104.4	403071.1	418959.8	210077.3	689006	634051.1	536035.7	499624.4	738711.3	349614.6	260218.8	396
25	M1197233	24954.87	23399.81	23575.95	13338.19	33246.27	26156.69	15766.12	25487.23	19042.66	18934.83	13620.29	20611.4	23869.51	22634.32	22294.85	22462.74	12240.95	19630.98	197
26	M119753	54103	49257.97	60770.72	35086.47	66681.28	52155.84	37296.66	35473.82	31866.72	32966.6	13828.12	58007.47	49774.35	45230.78	39611.76	59209.22	32914.16	21121.31	314
27	M121173	240164.2	3207662	331021.9	251582.1	277004.1	193025.7	438040.5	150957.3	230271.7	275420.5	293919	293830.4	231079.1	308697.2	220404.6	290114.2	414509.1	332537.5	2
28	M121173	2425847	174789.8	288869.6	240404.4	3378697	166736.2	3713308	2691870	165942.6	2600780	83681.79	282210.2	1992916	288429.7	322657.4	323585.8	2463562	2777134	30
29	M121176	352694.6	130687.2	426307.5	24478.46	418560.6	293284.8	413021.9	39924.64	42985.45	43437.39	56638.84	33514.14	57733.0	42693.03	70068.71	412904.2	53443.06	49367.68	706
30	M122768	140002.4	116594.1	158186.9	155712.5	94234.01	113308.7	126416.3	198397.4	115663.7	153246.4	129375.5	199662.6	117730.1	148161.3	116020.3	122180.6	113448.4	134329.7	883
31	M123746	144741.3	130602.7	171793	137241.2	165415.4	166985.3	177487.4	133245.3	128352.5	94373.31	149283.6	146908	158039.3	128054.9	142776.9	151719.7	126448	130698.8	131
32	M123732	88356.7	81693.14	76197.37	75632.53	86450.62	99250.24	65960.49	162082.1	76124.61	81249.24	106183.5	147584.7	82086.18	78140.29	71682.06	88380.97	144482.6	131978.6	107
33	M123753	1131755	1283104	867423.9	921317.9	1410529	1177023	900965.6	1433746	1260881	1421248	1462581	1320889	1370182	1275632	1148370	1337942	1696713	1797970	15
34	M123752	1177576	66355.3	56642.84	998293.2	75267.71	79438.89	60165.52	1323879	78001.79	83213.13	1705030	1184399	94035.13	78453.68	72901.28	86045.16	1623042	62782.46	105
35	M125767	179644.3	111714.3	51851.2	96462.24	160915.7	110145	109939.3	187179.6	47349.44	133821.7	189536.4	127374.3	118933.8	205647.3	130404.3	92409.4	179574.8	207092.8	250

[xcms.summary](#) Create a summary of XCMS analysis

**xcms.summary** Create a summary of XCMS analysis (Galaxy Version 1.0.3) Versions Options

**xset RData file**

output file from another function xcms (xcmsSet, group, retcor, fillpeaks etc.)

**Execute**



---

Este proyecto ha sido financiado con ayuda de la Comisión Europea.

La presente publicación recoge únicamente las opiniones de los autores, por lo que la Comisión no se hace responsable de cualquier uso que se haga de la información contenida en ella.

