BACKGROUND SUBTRACTION-MEDIATED DATA-DEPENDENT ACQUISITION

This application discloses a background subtraction-mediated data dependent acquisition method useful in mass spectrometry analysis. The method includes subtraction of background data from precursor ion spectra of a sample in real-time to obtain mass data of component(s) of interest and performs data-dependent acquisition on the component(s) of interest based on the resultant mass data from the background subtraction step. The present invention also encompasses mass spectrometer systems capable of background subtraction-mediated data-dependent acquisition and computer programs adapted for use in the background-subtraction-mediated data-dependent acquisition. The invention thus provides highly sensitive data-dependent acquisition for minor components of interest in a sample.
INTERNATIONAL SEARCH REPORT

International application No. PCT/US2012/021736

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - H01J 49/26 (2012.01)
USPC - 250/281

According to International Patent Classification (IPC) or to both national classification and IPC.

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - B01D 59/44; H01 J 49/00, 49/26 (2012.01)
USPC - 250/281, 282, 288

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, Google Patent Search, Google Scholar

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to-claim No.</th>
</tr>
</thead>
</table>

Further documents are listed in the continuation of Box C.

* Special categories of cited documents:
  "A" document defining the general state of the art which is not considered to be of particular relevance
  "E" earlier application or patent but published on or after the international filing date
  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  "O" document referring to an oral disclosure, use, exhibition or other means
  "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search: 06 July 2012

Date of mailing of the international search report: 13 JUL 2012

Authorized officer: Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300
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Form PCT/ISA/2 10 (second sheet) (July 2009)
**INTERNATIONAL SEARCH REPORT**

**Box No. II**  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. □ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. □ Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. □ Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III**  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See extra sheet

1. □ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. □ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ○ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ■ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-30

**Remark on Protest** □ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

□ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

□ No protest accompanied the payment of additional search fees.
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-30, drawn to a mass spectrometer system comprising data-dependent acquisition module comprising a mass data acquisition unit, a background subtraction module comprising a computing unit, wherein mass data acquisition by the datadependent acquisition module is mediated by the background subtraction module.

Group II, claims 31-54, drawn to a method of analyzing mass spectrum comprising an original mass spectrum of the sample at a chromatographic time point comprising m/z and intensity information of detected ion peaks, generating a current background-subtracted mass spectrum.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature of the Group I invention: data-dependent acquisition module, a background subtraction module wherein mass data acquisition by the datadependent acquisition module is mediated by the background subtraction module, as claimed therein is not present in the invention of Group II. The special technical feature of the Group II invention: an original mass spectrum of the sample at a chromatographic time point comprising m/z and intensity information of detected peaks, a current background-subtracted mass spectrum, as claimed therein is not present in the invention of Groups I.

Groups I and II lack unity of invention because even though the inventions of these groups require the technical feature of a mass spectrometer system comprising a data acquisition based on a peak, background data, subtracting background information from the acquired data, ion signals, this technical feature is not a special technical feature as it does not make a contribution over the prior art in view of US 2005/023061 A1 (DENNY et al) 20 October 2005 (20.10.2005) abstract; figure 1a; paragraphs 18-22; 61-62.

Since none of the special technical features of the Group I or II inventions are found in more than one of the inventions, unity of invention is lacking.