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[Continued on next page]

(54) Title: SINGLE-PROTEIN NANOMECHANICAL MASS SPECTROMETRY IN REAL TIME

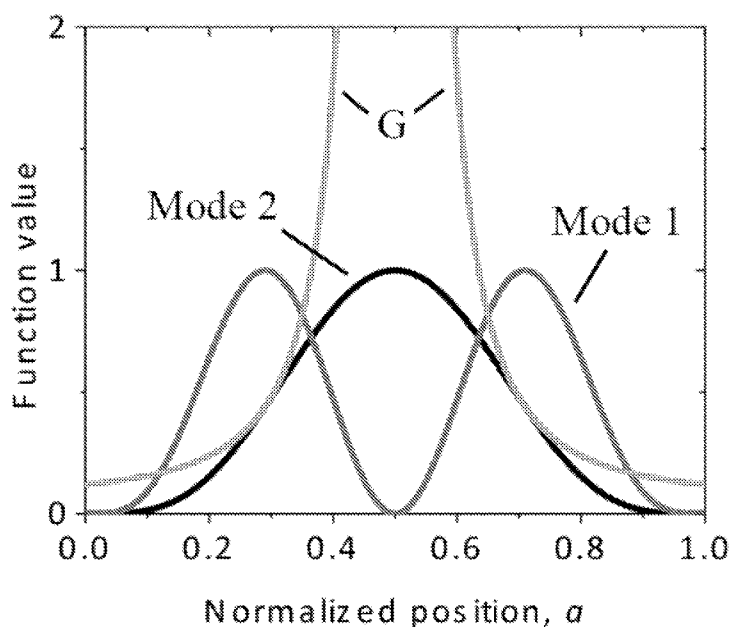


FIG. 4C

(57) Abstract: Methods and devices relating to measuring a landing position and mass of an analyte adsorbed to a nanomechanical resonator by resolving adsorbate-induced frequency shifts in at least two modes of a resonator resonance frequency, where during the resolving of the frequency shifts in the at least two modes analysis is so that the transformation (G) from the fractional-frequency shift pair to the analyte mass-position pair is one-to-one. Complex protein mixtures can be analyzed at high sensitivity and resolution.



TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:

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— *with international search report (Art. 21(3))*

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER

INV. H01J49/34 G01G3/16 G01N5/02 G01G9/00
ADD.

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)

H01J G01G G01N

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)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/261241 A1 (ROUKES MICHAEL L [US] ET AL) 22 October 2009 (2009-10-22) cited in the application paragraph [0059] - paragraph [0060] paragraph [0068] - paragraph [0074] figures 11-19 -----	1-8,17, 18,23-34
A	WO 2005/031300 A2 (PURDUE RESEARCH FOUNDATION [US]; BASHIR RASHID [US]; GUPTA AMIT KUMAR) 7 April 2005 (2005-04-07) page 19, line 13 - page 21, line 2 page 23, line 1 - page 28, line 9 figures 4-6 -----	1-8,17, 18,23-34



Further documents are listed in the continuation of Box C.



See patent family annex.

* 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

18 June 2014

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15/01/2015

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2013/040196

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2009261241	A1	22-10-2009	NONE

WO 2005031300	A2	07-04-2005	AU 2004276725 A1 07-04-2005
			CA 2530607 A1 07-04-2005
			EP 1651943 A2 03-05-2006
			WO 2005031300 A2 07-04-2005

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/040196

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 additional 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 an 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.:

1-8, 17, 18, 23-34

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-8, 17, 18, 23-34

Method for measuring a landing position and mass of an analyte adsorbed to a nanomechanical resonator wherein first and second driving signals generate a mix-down signal of mechanical origin at the readout electrode when the drive frequency matches exactly half of the resonance frequency.

2. claims: 9-16

Method for measuring a landing position and mass of an analyte adsorbed to a nanomechanical resonator wherein the transformation is a noise transformation.

3. claims: 19-22, 35-40

Method for measuring a landing position and mass of an analyte adsorbed to a nanomechanical resonator comprising method steps for delivering the analyte to the resonator or apparatus/method for measuring the mass of a sample using a LIAD delivery system
