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(54) Title: ASSAY APPARATUSES, METHODS AND REAGENTS

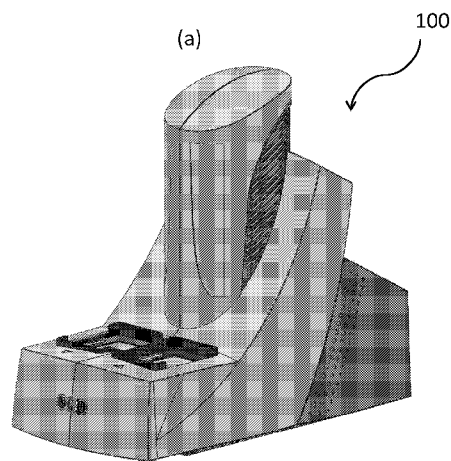


Fig. 1(a)-(b)

(57) Abstract: Apparatuses, systems, method, reagents, and kits for conducting assays as well as process for their preparation are described. They are particularly well suited for conducting automated analysis in a multi-well plate assay format. A method is provided for focusing an optical sensor to a spaced apart platform comprising the steps of: providing at least a higher, middle and lower patterned surface, wherein the middle patterned surface and the platform are aligned to each other and wherein a first distance between the higher and middle patterned surfaces and a second distance between the middle surface and lower patterned surface are substantially equal; obtaining a first difference in contrast values between the higher and middle patterned surfaces with the optical sensor; obtaining a second difference in contrast values between the middle and lower patterned surfaces with the optical sensor; and comparing the first and second differences in contrast values.



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- with international search report (Art. 21(3))
- 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))

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/10182

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 21/75, 21/76; C40B 60/12 (2014.01)

USPC - 436/48; 422/82.08; 250/214.1

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): G01N 21/75, 21/76, 33/00, 1/28; C40B 60/12, 30/00; H01L 27/148, 27/146; B08B 9/00; B01L 99/00 (2014.01)

USPC: 436/48; 422/82.08; 250/214.1, 208.1

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)

MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google Scholar; IEEE; ProQuest; Search terms used: focus, focal, optic, sensor, detector, assay, microassay, pattern, contrast, microtitre, microtiter, microplate, microwell, multiwell, upper, middle, lower, top, bottom, layer, surface

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7,842,246 B2 (WOHLSTADTER, J. et al.) November 30, 2010; figures 8B-14B, 10A-10B, 19-23, 35e, column 4, lines 46-64, column 11, lines 15-32, column 16, lines 54-67, column 17, lines 1-32, column 82, lines 1-16, column 104, lines 65-67, column 105, lines 1-28, column 116, lines 17-43, column 120, lines 20-67, column 121, lines 1-5, column 130, lines 39-52	1-7, 11-31 ---
Y		8-10
Y	US 8,173,332 B2 (KAMO, T. et al.) May 8, 2012; abstract	8-10
A	US 2007/0231217 A1 (CLINTON, C. et al.) October 4, 2007; entire document	1-31

☐ 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

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/10182

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:

-Please see Supplemental Page-

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.:
Group I: Claims 1-31

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.

---Continued from Box III: Observations where unity of invention is lacking---

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 fee must be paid.

Group I: Claims 1-31 are directed toward a method for focusing an optical sensor to a spaced apart platform comprising at least a higher, middle and lower patterned surface, a first distance, a second distance, a first contrast value difference, and a second contrast value difference.

Group II: Claims 32-81 and 123-161 are directed toward an instrument comprising a contact platform, wherein the contact platform comprises a plurality of interrogation zones, at least a pair of electrical contacts, a voltage potential, a controller, a voltage source, a multiplexer, P x Q matrix, a first alignment mechanism, a second alignment mechanism, a plate carriage platform, a plurality of apertures, a skirt, a latching mechanism, and a focusing mechanism.

Group III: Claims 82-110 are directed toward an instrument for conducting luminescence assays in a multi-well plate, the instrument comprising a light detection subsystem, a plate handling subsystem, a light-tight enclosure, a housing, a removable drawer, a housing top, a housing front, one or more plate introduction apertures, a detection aperture, a sliding light-tight door, a plurality of alignment features, an x-y subframe, a plurality of companion alignment features, a weight, one or more plate elevators, a plate lifting platform, a plate translation stage, a plate carriage, an opening, one or more plate stackers, a light detector, and a light-tight seal.

Group IV: Claims 111-122 are directed toward an instrument for conducting luminescence assays in a multi-well plate, the instrument comprising a plate handling subsystem, a plate carriage, a frame, a plate latching mechanism, a plate carriage ledge, a plate clamp arm, a proximate, a distal end, an x-y plate, an upper clamp, an angled surface, a plate positioning element, a rod, a pedal, a spring, a plate wall, a lower plate clamp, a multi-well plate skirt, and a lower plate clamp ramp.

Group V: Claims 162-169 are directed toward an apparatus for measuring luminescence from a multi-well plate of a plate type selected from the group consisting of a single well addressable plate or a multi-well addressable plate, the apparatus comprising a plate type identification interface, a plate translation stage, a plate contact mechanism, a plurality of contact probes, the range of motion of the stage, a contact mechanism elevator, a bottom contact surface, a voltage source, an imaging system, and a P x Q matrix of wells.

The inventions listed as Groups I-V 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. Groups I has at least a middle patterned surface, a first distance, a second distance, a first contrast value difference, a second contrast value difference that Groups II-V do not have. Group II has at least a plurality of interrogation zones, a controller and a multiplexer that Groups I and III-V do not have. Group III has at least a removable drawer, a sliding light-tight door, weight, one or more plate stackers, light detector, and a light-tight seal that Groups I, II, IV, and V do not have. Group IV has at least a plate clamp arm, an upper clamp, a rod, pedal, lower clamp plate, and a lower plate clamp ramp that Groups I-III and V do not have. Group V has at least a single-well addressable plate, plate type identification interface, a plurality of contact probes, a contact mechanism elevator, and an imaging system that Groups I-IV do not have.

The common technical features of Groups I-V are at least focusing an optical sensor, an instrument for conducting luminescence in a multi-well plate in a P x Q matrix, alignment features, plurality of apertures, plate carriage, and plate handling subsystem. These common features are disclosed by US 7,842,246 B2 to Wohlstadter et al. (hereinafter Wohlstadter). Wohlstadter discloses focusing an optical sensor (optics 1708 for focusing light onto a photodetector 1706, figure 17, column 78, lines 59-62), an instrument for conducting luminescence in a multi-well plate in a P x Q matrix (multi-well assay plate 1710 in a P x Q matrix conducting electrochemiluminescent assays in reader 1700, figure 17, column 78, lines 11-36 and column 79, lines 14-22), alignment features (plate alignment mechanism 1712, figure 17, column 78, lines 10-36), plurality of apertures (apertures 1714, figure 17, column 78, lines 11-49), plate carriage (plate carrier 1740, figure 17, column 78, lines 11-36), and plate handling subsystem (plate transport mechanism 1716, figure 17, column 78, lines 11-36).

Since the common technical feature is previously disclosed by the Montena reference, these common features are not special and so Groups I-V lack unity.