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16/864,744	05/01/2020	Emil P. Kartalov	88DG-330783-US4	9929
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SHEPPARD, MULLIN, RICHTER & HAMPTON LLP			EXAMINER	
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			ART UNIT	PAPER NUMBER
			1672	
			NOTIFICATION DATE	DELIVERY MODE
			05/10/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 16/864,744	Applicant(s) Kartalov et al.	
	Examiner RUSSELL S NEGIN	Art Unit 1672	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 28 March 2023.
 ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☒ Claim(s) 21-40 is/are pending in the application.
 5a) Of the above claim(s) ____ is/are withdrawn from consideration.

6) ☐ Claim(s) ____ is/are allowed.

7) ☒ Claim(s) 21-40 is/are rejected.

8) ☐ Claim(s) ____ is/are objected to.

9) ☐ Claim(s) ____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10) ☐ The specification is objected to by the Examiner.

11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
Certified copies:
 a) ☐ All b) ☐ Some** c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
 Paper No(s)/Mail Date ____.

3) ☐ Interview Summary (PTO-413)
 Paper No(s)/Mail Date ____.

4) ☐ Other: ____.

DETAILED ACTION

Comments

The present application is being examined under the pre-AIA first to invent provisions. In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

Claims 21-40 are pending and examined in the instant Office action.

Information Disclosure Statement

The IDS filed on 12/27/2022 has been considered.

Withdrawn Objections/Rejections

The objections to the claims are withdrawn in view of amendments filed to the instant set of claims on 28 March 2023.

The rejections of the claims under 35 U.S.C. 112 are withdrawn in view of amendments filed to the instant set of claims on 28 March 2023.

Claim Rejections - 35 USC § 103

The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under pre-AIA 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of pre-AIA 35 U.S.C. 103(c) and potential pre-AIA 35 U.S.C. 102(e), (f) or (g) prior art under pre-AIA 35 U.S.C. 103(a).

The following rejection is reiterated:

35 U.S.C. 103 Rejection #1:

Claims 21-25, 27, 29-30, and 32-40 is/are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Han et al. [Nature Biotechnology, volume 19, 2001, pages 631-835; on IDS] in view of Lin et al. [WO 2012/058628 A2; on IDS].

Claim 21 is drawn to an assay that is capable of unambiguously detecting the presence or absence of each of at least M analytes. The assay requires that each of the M analytes is encoded as a value of one component of a fluorescent signal. The assay requires that the fluorescent signal comprises F wavelength components. The assay is capable of detecting the presence or absence of each of the at least M analytes, in any combination of presence or absence, in a single sample volume without

immobilization, separation, mass spectrometry, or melting curve analysis, based on detection of the F wavelength components. M is greater than F.

Claim 32 is further limiting requiring the coding scheme to be innately non-degenerate or non-degenerate by construction.

Claims 34-36 are drawn to similar subject matter as claim 32, except as a kit.

The document of Han et al. studies quantum-dot tagged microbeads for multiplexed optical coding of biomolecules [title]. Figure 5 of Han et al. illustrates four oligonucleotides analytes (M=4) attached to microbeads with different combinations of 3 types of quantum dots- red, green, and blue (F=3). The type of optical code as a result of spectroscopy indicates the type of analyte being examined. Han et al. does not use immobilization, separation, mass spectrometry, or melting curve analysis.

Han et al. does not teach detecting cumulative non-degenerate combinations of analytes.

The document of Lin et al. studies nucleic acid nanostructure barcode probes [title]. Figure 2 of Lin et al. illustrates the cumulative non-degenerate combination of each of 27 different combinations of the three fluorophores (R, G, and B) within an image. Pages 7 and 8 of Lin et al. describe Figure 2 of Lin et al.

With regard to claims 22-23, Han et al. and Lin et al. teach red, green, and blue components to the signal. Figure 6 of Han et al. illustrates a range of intensities associated with each component.

With regard to claims 24-25 and 37-39, Figure 5 of Han et al. illustrates hybridization probes for different analytes wherein each analyte comprises a different combination of fluorophores. Figure 2 of Lin et al. teaches that the number of hybridization probes is greater than the number of analytes.

With regard to claim 27, Figure 5 of Han et al. illustrates three components of the signals used to detect each analyte.

With regard to claim 29, Figure 5 of Han et al. teaches that each analyte comprises a polynucleotide.

With regard to claim 30, page 31 of Lin et al. teaches the presence of a computer to analyze spectral data.

With regard to claims 32-33, Figure 2 of Lin et al. teaches a histogram of non-degenerate counts of presence the 27 different combinations of fluorophores in an image.

With regard to claim 40, the different sizes of the bars in the histogram in Figure 2 of Lin et al. teaches that the analyte specific reagents are each present at a different amount.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quantum dot hybridization assay of Han et al. by use of the cumulative non-degenerate fluorophore assay of Lin et al. wherein the motivation would have been that the cumulative and non-degenerate nature of the assay of Lin et al. adds mathematical and empirical tools to the assay of Han et al. [Figure 2 of Han et al.]. There would have been a reasonable expectation of success in combining Han et al. and Lin et al. because both studies analogously pertain to assays involving colored fluorophores or quantum dots.

Response to arguments:

Applicant's arguments filed 28 March 2023 have been fully considered but they are not persuasive.

Applicant argues that the beads of Han et al. are immobilized on a glass slide. While a subset of beads are localized on a glass slide for the purpose of experimental measurement, the common state of the glass particles is immobilized in solution.

In response to applicant's argument that the references fail to show certain features of the invention, it is noted that the features upon which applicant relies (i.e. a single cumulative measurement) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the prior art does not teach eliminating degeneracy. This argument is not persuasive because Figure 2 of Lin et al. illustrates the cumulative non-

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degenerate combination of each of 27 different combinations of the three fluorophores (R, G, and B) within an image.

Applicant argues that Lin et al. does not teach a technique to measure presence and absence combination without immobilization, mass spectrometry, or melting curve analysis. This is an obviousness prior art rejection, and Han et al. is relied upon to teach this limitation.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #2:

Claims 26 and 31 is/are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Han et al. in view of Lin et al. as applied to claims 21-25, 27, 29-30, and 32-40 above, in further view of Albani et al. [US PG PUB 2006/0039918 A1].

Claim 26 is further limiting wherein the signal is generated during PCR.

Claim 31 is further limiting wherein the assay is performed using a computer and thermal cycler.

Han et al. and Lin et al. make obvious fluorophore and quantum dot assays to detect presence and absence of analytes, as discussed above.

Han et al. and Lin et al. do not teach PCR, computers, and thermal cyclers.

The document of Albani et al. studies stress proteins and peptides [title].

Paragraph 184 of Albani et al. relates fluorophores, PCR, and thermal cyclers.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quantum dot hybridization assay of Han et al. and the cumulative non-degenerate fluorophore assay of Lin et al. by use of the PCR,

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computers, and thermal cyclers of Albani et al. wherein the motivation would have been that Albani et al. adds empirical tools that facilitate the analysis of fluorophores [paragraph 184 of Albani et al.].

Response to arguments:

Applicant's arguments filed 28 March 2023 have been fully considered but they are not persuasive.

Applicant argues that Albani et al. does not overcome the alleged deficiencies of the initial obviousness prior art rejection. Since the initial obviousness prior art rejection is not deficient, this argument is not persuasive.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #3:

Claim 28 is/are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Han et al. in view of Lin et al. as applied to claims 21-25, 27, 29-30, and 32-40 above, in further view of Hardin et al. [US PG PUB 2010/0317005 A1].

Claim 28 is further limiting wherein the fluorescence signals are used to generate chromatograms.

Han et al. and Lin et al. make obvious fluorophore and quantum dot assays to detect presence and absence of analytes, as discussed above.

Han et al. and Lin et al. do not teach using fluorescence signals to generate chromatograms.

The document of Hardin et al. studies modified nucleotides [title]. Paragraph 143 of Hardin et al. relates fluorescence signals to chromatograms.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the quantum dot hybridization assay of Han et al. and the cumulative non-degenerate fluorophore assay of Lin et al. by use of the chromatograms of Hardin et al. wherein the motivation would have been that Hardin et al. adds empirical tools that facilitate the analysis of fluorophores [paragraph 143 of Hardin et al.].

Response to arguments:

Applicant's arguments filed 28 March 2023 have been fully considered but they are not persuasive.

Applicant argues that Hardin et al. does not overcome the alleged deficiencies of the initial obviousness prior art rejection. Since the initial obviousness prior art rejection is not deficient, this argument is not persuasive

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have

been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

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The following rejection is reiterated:Double Patenting Rejection #1:

Claims 21, 23, 26, 27, and 29-34 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 3, 7-8, 11-12, 15-17, and 20, respectively, of U.S. Patent No. 8,838,394. Although the claims at issue are not identical, they are not patentably distinct from each other because both sets of claims are drawn to assays for detection cumulative presence/absence patterns of analytes associated with fluorophores without using immobilization or mass spectrometry. While the claims of '394 recite more limitations than the instantly rejected claims, the claims of '394 anticipate the instantly rejected claims.

Response to arguments:

Applicant requests the double patenting rejection be held in abeyance.

The following rejection is reiterated:Double Patenting Rejection #2:

Claims 21, 26, and 30-31 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 4-5, and 9, respectively, of U.S. Patent No. 10,068,051 B2. Although the claims at issue are not identical, they are not patentably distinct from each other because both sets of claims are drawn to assays for detection cumulative presence/absence patterns of analytes associated with fluorophores without using immobilization or mass spectrometry. While the claims of

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'394 recite more limitations than the instantly rejected claims, the claims of '051 anticipate the instantly rejected claims.

Response to arguments:

Applicant requests the double patenting rejection be held in abeyance.

The following rejection is reiterated:

Double Patenting Rejection #3:

Claims 21, 26, and 30 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 7, and 13, respectively, of U.S. Patent No. 10,770,170 B2. Although the claims at issue are not identical, they are not patentably distinct from each other because both sets of claims are drawn to assays for detection cumulative presence/absence patterns of analytes associated with fluorophores without using immobilization or mass spectrometry. While the claims of '394 recite more limitations than the instantly rejected claims, the claims of '170 anticipate the instantly rejected claims.

Response to arguments:

Applicant requests the double patenting rejection be held in abeyance.

Related Prior Art

The prior art of Geiss et al. [WO 2008/124847; on IDS] teach targeting sequences using coding via labeling. However, Geiss et al. does not teach the technique in the recited claims.

E-mail Communications Authorization

Per updated USPTO Internet usage policies, Applicant and/or applicant's representative is encouraged to authorize the USPTO examiner to discuss any subject matter concerning the above application via Internet e-mail communications. See MPEP 502.03. To approve such communications, Applicant must provide written authorization for e-mail communication by submitting the following statement via EFS-Web (using PTO/SB/439) or Central Fax (571-273-8300):

Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with the undersigned and practitioners in accordance with 37 CFR 1.33 and 37 CFR 1.34 concerning any subject matter of this application by video conferencing, instant messaging, or electronic mail. I understand that a copy of these communications will be made of record in the application file.

Written authorizations submitted to the Examiner via e-mail are **NOT** proper. Written authorizations must be submitted **via EFS-Web** (using PTO/SB/439) **or Central Fax** (571-273-8300). A paper copy of e-mail correspondence will be placed in the patent application when appropriate. E-mails from the USPTO are for the sole use of the intended recipient, and may contain information subject to the confidentiality requirement set forth in 35 USC § 122. See also MPEP 502.03

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. This Examiner can normally be reached from Monday through Thursday from 8 am to 3 pm and variable hours on Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Larry Riggs, Supervisory Patent Examiner, can be reached at (571) 270-3062.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

/RUSSELL S NEGIN/
Primary Examiner, Art Unit 1672
6 May 2023