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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/243,585	10/01/2008	Robert A. Ach	20080261-01	1470

22878 7590 07/11/2016

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EXAMINER	
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ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
07/11/2016	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ROBERT A. ACH and N. ALICE YAMADA

Appeal 2013-009191
Application 12/243,585
Technology Center 1600

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and RICHARD J. SMITH, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This appeal under 35 U.S.C. § 134(a) involves claims 1 and 4–15 (*see generally* Ans. 3).[2] Examiner entered rejections under 35 U.S.C. § 101 and 35 U.S.C. § 103(a). We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] Appellants identify the Real Party in Interest as "Agilent Technologies, Inc." (App. Br. 3.)

[2] "Claims 16–20 [stand] withdrawn from further consideration . . . as being drawn to a nonelected invention" (Ans. 3).

STATEMENT OF THE CASE

The claims are directed to "a method of sample analysis" (Spec. 1). Claim 1 is representative and reproduced in the Claims Appendix of Appellants' Brief.

Claims 1 and 4–15 stand rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter.

Claims 1 and 4–15 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Hyldig-Nielsen,[3] Tafas,[4] Ishiguro,[5] and Appellants' admitted prior art.

Utility:

ISSUE

Does the evidence of record support Examiner's finding that Appellants' claimed invention is directed to non-statutory subject matter?

FACTUAL FINDINGS (FF)

FF 1. Examiner finds that Appellants' claimed methods requirethe use of "probes" that "hybridize to different RNA molecules of [a] microbe at sites that are unique to [the] microbe" and that "RNA has a naturally-occurring relationship with [a microbial] cell," wherein the RNA "sequence [has] a naturally-occurring ordering of nucleotides found within the genetic material of each microbe" (Ans. 8).

FF 2. Examiner finds that Appellants' "claimed method fairly encompasses any of the admittedly well-known and routine conditions

[3] Hyldig-Nielsen et al., US 2006/0003332 A1, published Jan. 5, 2006.
[4] Tafas et al., US 2008/0213769 A1, published Sept. 4, 2008.
[5] Ishiguro et al., US 7,112,407 B2, issued Sept. 26, 2006.

where *in situ* hybridization of probes to different RNA molecules occurs" (Ans. 8–9; *see also id.* at 22).

FF 3. Examiner finds that, for the reasons set forth in the obviousness rejection below, "the use of oligonucleotide probes, including those that are differently labeled, was routine in the art at the time of filing" (Ans. 9).

FF 4. Examiner finds that "the aspect of using *in situ* hybridization conditions,' [together with] reading and determining [steps,] amount to instructions that are well-understood, routine, conventional activity, previously engaged in by those in the field [and] add nothing specific to the natural principle that would render it patent-eligible" (Ans. 9; *see generally id.* at 22 (Appellants' "claimed method does not specify the conditions under which the hybridization is to take place [or the] conditions under which one is to perform the step of 'reading said contacted sample,' much less require any device to perform any one or combinations of steps recited in the claimed method")).

FF 5. Examiner finds that Appellants' Specification discloses that the selection of labels, such as fluorophores, that "do not interfere with the detection characteristic of any other label" are known in the art (Ans. 9, citing Spec. 25).

FF 6. Examiner finds that the term "microbe" encompasses "any microbe, be it bacteria and/or virus[], including those that are known as well as those that are yet to be discovered (Ans. 10; *see also id.* at 8).

FF 7. Examiner finds that Appellants' "probe set" encompasses "probes that are known as well as unknown, and that the labels and their associated signals encompass that which is known and that which is yet to be discovered" (Ans. 10; *see also id.* at 22).

ANALYSIS

Examiner finds that Appellants': "claim[ed] the[ir] invention in such general terms, [that] the claims fairly encompass embodiments that are not only known, but also seek to block future development in the area of art" and "claimed method is deemed to focus on the use of natural laws and does not 'also contain other elements or a combination of elements . . . to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself'" (Ans. 11). We are not persuaded.

Appellants' claimed method requires, *inter alia*, the use of a first and second population of labeled oligonucleotides that produce first and second distinguishable signals, respectively (*see* Appellants' claim 1). Appellants' claimed method further requires that the identity of a microbe is determined "on the basis of [a] predetermined optically detectable signature" (Appellants' claim 1). The method of Appellants' claim 1 defines a "predetermined optically detectable signature" as "a composite signal of said first and second signals" (*id.*).

Examiner established that labeled oligonucleotides that meet the foregoing criteria are known in the art (*see* FF 5). Examiner did not, however, establish that such labeled oligonucleotides were naturally occurring, mental processes, or abstract intellectual concepts (*cf.* Ans. 6, citing *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289, 1293 (2012) ("Phenomena of nature . . ., mental processes, and abstract intellectual concepts are not patentable").

Examiner does not address and, thereby, failed to establish that the steps of Appellants' claimed method, which, *inter alia*, require the production of a composite signal of a first and second signal to obtain an

optically detectable signature that is used to identify a microbe fails to transform the use of natural phenomena (i.e. the sequence of microbial mRNA) or known reagents (i.e. labeled probes) into patent-ineligible subject matter. *Id.* at 1294. Thus, on this record, Examiner failed to establish that Appellants' claimed subject matter, when read as a whole, is nothing more than a recitation of "a nonpatentable phenomenon, process, or concept" with the additional "words 'apply it'." *Id.*; *see* Ans. 6 and 8. For the same reasons, Examiner failed to establish that Appellants' claimed invention, when read as a whole, is nothing more than "post-solution activity that is purely conventional or obvious." *Id.* at 1299.

As Appellants explain, their:

> claims are directed to a method in which a microbe is hybridized in situ with a particular set of labeled oligonucleotides that produce a composite signal. Specifically, the claims use oligonucleotides (which are man-made), the hybridization is done *in situ* (which does not happen in nature), and the signal produced is a composite signal (which does not occur in nature).

(App. Br. 5; *see* Reply Br. 2–3.)

CONCLUSION OF LAW

The evidence of record fails to support Examiner's finding that Appellants' claimed invention is directed to non-statutory subject matter. The rejection of claims 1 and 4–15 under 35 U.S.C. § 101 as directed to non-statutory subject matter is reversed.

Obviousness:

ISSUE

Does the preponderance of evidence relied upon by Examiner support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 8. Hyldig-Nielsen discloses "PNA probes, probe sets, methods and kits useful for detecting, identifying and/or quantitating one or more organisms of interest in a sample wherein the organisms are members of the bacterial species of *E. coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Pseudomonas cepatia*, *Pseudomonas fluorescens* or organisms of a bacterial genus including the *Salmonella* genus, *Bacillus* genus or *Pseudomonas* genus" (Hyldig-Nielsen ¶ 10; Ans. 14–15; *see also* Ans. 19–20, citing Appellants' admissions).

FF 9. Hyldig-Nielsen's "PNA probes . . . may comprise . . . detectable moieties (labels)," which "are used in in-situ hybridization (ISH) and fluorescence in-situ hybridization (FISH) assays" (Hyldig-Nielsen ¶¶ 46 and 47; *see also id.* ¶ 31; Ans. 15–16; *see* Ans. 20, citing Appellants' admissions).

FF 10. Hyldig-Nielsen discloses the use of "one or more distinct independently detectable moieties . . . to label two or more different probes . . . in an assay," wherein

> the ability to differentiate between and/or quantitate each of the independently detectable moieties provides the means to multiplex a hybridization assay because the data which correlates with the hybridization of each of the distinctly (independently) labeled probe to a particular nucleic acid

> sequence can be correlated with the presence, absence or quantity of each organism sought to be detected in the sample.

(Hyldig-Nielsen ¶ 35; Ans. 15.)

FF 11. Hyldig-Nielsen's "multiplex assays . . . may be used to simultaneously detect the presence, absence or quantity of two or more organisms in the same sample and in the same assay" (Hyldig-Nielsen ¶ 35; *see also id.* ¶ 62; Ans. 16).

FF 12. Hyldig-Nielsen discloses "[t]he grouping of PNA probes within probe sets to be used with methods for detecting specific groups of organisms (e.g., classification within species, genus, or USP bacteria)" (Hyldig-Nielsen ¶ 62; Ans. 16).

FF 13. Examiner finds that Hyldig-Nielsen fails to disclose the use of "probes to RNA that is not rRNA" and relies on Ishiguro to disclose the "detection of bacterial mRNA via hybridization reaction" (Ans. 17 and 19).

FF 14. Examiner finds that Hyldig-Nielsen fails "to teach basing the determination of a specific bacteria . . . on a pattern of signals emanating from a single bacterial cell" and relies on Tafas to make up for this deficiency in Hyldig-Nielsen (Ans. 18).

FF 15. Examiner finds that Tafas discloses "fluorescence *in situ* hybridization (FISH)," wherein a "multicolor probe set . . . permit[s] simultaneous analysis of [] three genomic markers within a single cell" (Ans. 17; Tafas ¶ 17; *see also* Ans. 24–25).

FF 16. Appellants contend that a "composite signal" can be detected as two separate signals or as a single signal which is a combination of two separate signals, wherein:

> Using [] Examiner's example, if purple is detected, then red and blue signals must be present[, i.e., purple is a combination of

> red and blue]. Alternatively, one could detect red and blue signals separately, which would also indicate that red and blue signals are present. Composite signals can be detected both ways")

(App. Br. 8.)

FF 17. Appellants' Specification discloses that an "'[o]ptically detectable signature' may be made up of one or more signals, where the signal(s) is produced by a label(s). An optically detectable signature may be made up of: a single signal, a combination of two or more signals, ratio of magnitude of signals, etc." (Spec. 6:16–21).

FF 18. Appellants' Specification discloses that "[t]he hybridization of [the label] set to a target microbe provides an optically detectable signature to the microbe where the signature is the combination of the first and the second signal" (Spec. 11:1–3).

FF 19. Appellants' Specification discloses that "each microbe has a different signature comprised of [] different combination[s] of signals" (Spec. 13:5–6).

FF 20. Appellants' Specification discloses that the "'distinguishable labels'" used for the probes "can be independently detected and measured, even when the labels are mixed. In other words, the amounts of label present (e.g., the amount of fluorescence) for each of the labels are separately determinable, even when the labels are co-located (e.g., in the same tube or in the same duplex molecule or in the same cell)."

ANALYSIS

Based on the combination of Hyldig-Nielsen, Tafas, Ishiguro, and Appellants' admitted prior art, Examiner concludes that, at the time Appellants' invention was made, it would have been prima facie obvious "to

use a combination of [labeled] probes that hybridize to a nucleotide sequence [(i.e. RNA that is not rRNA)] that is conserved across variants of a given species . . .[,] whereby identification of the specific organism is based upon the pattern of labels/signals detected" (Ans. 18–19). In this regard, Examiner finds that Hyldig-Nielsen discloses "that one can use a combination of probes that hybridize [in situ] to nucleic acids in a common bacterial cell and that the detection can result in the identification of species" and Tafas discloses "that one can use a plurality of probes, each bearing a different label, in a common assay where simultaneous hybridization to different nucleic acids in a common cell is conducted" (Ans. 18; *see also id.* at 20–21).

Appellants contend that Hyldig-Nielsen suggests a "'one fluorophore = one microbe' system," which fails to suggest a "composite signal of the first and second signals" as is required by Appellants' claimed invention (App. Br. 10–11; *cf.* FF 14). In this regard, Appellants contend that Examiner failed to establish that Ishiguro makes up for the foregoing deficiency in Hyldig-Nielsen (App. Br. 12). Appellants further contend that Tafas does not provide a "composite signal" (App. Br. 11–12).

Appellants contend that "Tafas' ¶ 17 [] is the only paragraph[, in Tafas,] that refers to a multicolor probe set that can be used to identify three markers within a cell" (App. Br. 11; *see* FF 15). In this regard, Appellants contend that "Tafas fails to provide . . . a signal that is a composite of two other signals" (App. Br. 11). Instead, Appellants contend, Tafas discloses

> that the multicolor probe set referred to in [Tafas' ¶ 17] contains three probes, each labeled with a different fluorophore (where the emitted colors are referred to as "orange", "green" and "aqua"). The different probes hybridize to different parts

> of chromosome 8 to produce a . . . signal pattern (i.e., a pattern that has two green bands sandwiched between two orange bands and two aqua bands).

(App. Br. 11.) Therefore, Appellants contend that "Tafas teaches away from using composite signals because [Tafas'] method relies on an ability to distinguish the different fluorophores separately from one another in order to identify [] cells" (*id.*). We are not persuaded.

Appellants concede that their Specification "does not contain an explicit definition for what is meant by the term 'composite signal'" (App. Br. 7). Nonetheless, Appellants contend that a "composite signal" can be detected as two separate signals or as a single signal which is a combination of two separate signals (FF 16). Thus, as Examiner explains, Appellants' contention regarding Tafas "is in direct conflict with what [A]ppellant's [sic] representative [] asserted at page 8 of the Brief" (Ans. 25; *cf.* FF 16).

For the foregoing reasons, we are not persuaded by Appellants' contention that the term "'composite signal' . . . should be interpreted as a 'blend' of two or more other signals" or that Tafas' "chromosome banding pattern that contains different colored bands is not a 'composite signal'" (Reply Br. 3 and 4).

We are not persuaded by Appellants' contention that Examiner "interpreted the term 'composite signal' in a way that is not consistent [with Appellants'] [S]pecification" (Reply Br. 4). To the contrary, Examiner interpreted the term in a manner that is consistent with Appellants' interpretation of the term, which is not defined by their Specification (*see* FF 16; *see also* App. Br. 7). We recognize, but are not persuaded by Appellants' contention that, when read in light of their Specification the undefined term "composite signal" is clear to a person of ordinary skill in

this art and "has a plain meaning in the English language," which is contrary to Examiner's interpretation of the term (Reply Br. 5; FF 17–20).

Notwithstanding Appellants' contentions to the contrary, Examiner provided Appellants an opportunity to interpret the term "composite signal" in light of their Specification (*see* July 30, 2012 Office Action 9 (wherein Examiner rejected Appellants claimed invention under the second paragraph of 35 U.S.C. 112 as "indefinite with respect to what constitutes the metes an bounds of a 'composite signal of said first and second signals'")). In response, Appellants contended that when interpreted in light of their Specification, the term "composite signal" means that a signal can be detected as two separate signals or as a single signal which is a combination of two separate signals (FF 16). Relying upon Appellants' definition of the term composite signal, Examiner withdrew the rejection under 35 U.S.C. 112, second paragraph (*see* Ans. 4).

Thus, notwithstanding Appellants' contentions to the contrary, the combination of Hyldig-Nielson, Tafas, and Ishiguro makes obvious the subject matter of Appellants' claim 1.

CONCLUSION OF LAW

The preponderance of evidence relied upon by Examiner supports a conclusion of obviousness. The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over the combination of Hyldig-Nielson, Tafas, and Ishiguro is affirmed. Claims 4–15 are not separately argued and fall with claim 1.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED