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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SAM KAVUSI and CHRISTOPH LANG

Appeal 2017-004649
Application 12/895,361
Technology Center 1600

Before JEFFREY N. FREDMAN, JOHN E. SCHNEIDER, and DAVID COTTA, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1] under 35 U.S.C. § 134 involving claims to a method of providing a confidence test for an assay. The Examiner rejected the claims as obvious and as directed to non-statutory subject matter. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Statement of the Case

Background

"[M]ultiplexed measurement platforms such as protein arrays are a promising diagnostic technology that are currently being explored in

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[1] Appellants identify the Real Party in Interest as Robert Bosch GmbH (*see* App. Br. 2).

conducting the diagnostic tests" (Spec. ¶ 3). "Various approaches to mitigate the errors encountered when using multiplexed measurement platforms have been developed including the provision of a coefficient of variation indicative of the consistency between various test sites on a platform or the consistency between various platforms" (Spec. ¶ 8).

According to Appellants

> a need exists for a device and method of providing a confidence test for an assay. A further need exists for providing a quality metric for assays such as multiplexed assays, e.g., protein arrays, competitive assays, or bead based arrays, as well as low cost devices, e.g., lateral flow devices, or other biochips

(Spec. ¶ 11).

The Claims

Claims 1–13 and 23 are on appeal. Independent claim 1 is representative and reads as follows:

> 1. A method of providing a confidence test for an assay comprising:
>
> determining, using a control sample having a known amount of molecules of interest, a first quality metric for the molecule of interest indicative of a variation in a proportion of the molecules of interest in the control sample that are bound at each of a first and a second thermodynamic state, wherein the first and second thermodynamic state are associated with a respective first test environment and second test environment wherein the second test environment is different from the first test environment;
>
> exposing an uncontrolled sample having an unknown amount of the molecules of interest to a plurality of test sites on an assay device, each of the plurality of test sites configured to bind the molecule of interest;

establishing the first test environment at a first of the plurality of test sites on the assay device;

establishing the second test environment at a second of the plurality of test sites on the assay device;

obtaining a first detection signal associated with the first of the plurality of test sites exposed to the uncontrolled sample and at the first test environment;

obtaining a second detection signal associated with the second of the plurality of test sites exposed to the uncontrolled sample and at the second test environment;

determining a second quality metric for the molecule of interest indicative of a variation in a proportion of the molecules of interest in the uncontrolled sample that are bound at each of two thermodynamic states based upon the first detection signal and the second detection signal;

comparing the second quality metric with the first quality metric;

quantifying the amount of the molecules of interest using at least one of the first detection signal and the second detection signal; and

determining a confidence in the quantified amount of the molecules of interest based upon the comparison of the second quality metric with the first quality metric.

The Issues

A. The Examiner rejected claims 1–13 and 23 under 35 U.S.C. § 101 as being directed to non-statutory subject matter (Final Act. 3–8).

B. The Examiner rejected claims 1–13 and 23 under 35 U.S.C. § 103(a) as obvious over Pi[2] (Final Act. 9–14).

A. 35 U.S.C. § 101

The Examiner rejects all of the claims on appeal under 35 U.S.C. § 101 as being directed to patent-ineligible subject matter, specifically "a series of abstract data processing steps" (Final Act. 4). The Examiner finds the claim steps of "determining a second quality metric . . . based upon the first detection signal and the second detection signal" and "comparing the second quality metric with the first quality metric" are abstract (*id.*).

The Examiner also finds the claims "encompass a natural relationship pertaining to any 'quality metric of interest indicative of a variation in a proportion of the molecules of interest in a control sample that are bound at each of a first and second thermodynamic state'" (Final Act. 3). The Examiner finds this element falls into the "category of natural phenomena" (*id.*).

The Examiner reaches these conclusions by applying the test set out in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012) (Final Act. 3–8) based on the two-step *Alice* framework. *Alice Corp. Pty. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014).

Appellants contend "the claim does not monopolize an abstract idea. For example, the preamble of claim 1 limits the scope of claim. Claim 1 recites 'a confidence test for an assay'. Thus, not all confidence tests fall

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[2] Pi, WO 2007/067819 A2, published June 14, 2007. Because the Examiner and Appellants both cite to the Pi, US 8,673,650 B2, issued Mar. 18, 2014 (*see, e.g.*, Ans. 9 and App. Br. 22), we will also cite to the '650 patent as ("Pi").

within the scope of the claim, only confidence tests of assays" (App. Br. 14). Appellants contend "the uncontrolled sample must . . . be exposed to the two test sites, and detection signals obtained from the two test sites. Even without more, the limitations associated with obtaining the signals related to the uncontrolled sample are sufficient to pass muster under 35 U.S.C. § 101" (*id.* at 15). Appellants contend:

> claim 1 requires 1) identifying a molecule of interest (arguably abstract), 2) determining a quality metric for the molecule of interest by using a controlled sample, 3) the quality metric must be related to two different dynamic states of the molecule of interest, 4) each of the dynamic states must be associated with a respective one of the two test environments, and 5) the two test environments must differ in some respect. Finally, the obtained signals must be used to generate a metric which is indicative of a variation in a proportion of the molecules of interest in a control sample that are bound. All of these limitations further limit the scope of the claim.
>
> After all of the foregoing, yet another quality metric is determined for the molecule of interest in the uncontrolled sample "bound at each of two thermodynamic states based upon the first detection signal and the second detection signal".
>
> Thus, claim 1 requires significantly more than simply encoding an abstract idea into a computer program as was determined to be the case in *Alice*.

(*Id.* at 15–16).

To determine whether a claim is invalid under § 101, we employ the two-step *Alice* framework. In step one, we ask whether the claims are directed to a patent ineligible concept, such as an abstract idea or law of nature. *Alice*, 134 S. Ct. at 2355; *Mayo*, 566 U.S. at 75–77; *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015).

While method claims are generally eligible subject matter, method claims that are directed only to abstract ideas and/or natural phenomena are directed to a patent ineligible concept. *Ariosa*, 788 F.3d at 1376.

Alice Step One

We have reviewed the Examiner's determinations, and we agree that claim 1 is directed to the abstract idea of data processing according to a rule based system. The Examiner's determinations are adequately supported by the intrinsic evidence. Neither the claims nor the Specification provide any technological improvements to the mechanics of detecting molecules in different test environments.

Rather, as the Examiner found, the claims combine molecule detection with a "series of abstract data processing steps" to obtain comparative "quality metrics" that are used for determining a "confidence test" for reliability of an assay. *See* claim 1, Ans. 3. We agree with the Examiner that data processing to determine two mathematical "quality metrics" and a resultant "confidence test" is abstract, both as a matter of mathematical relationships and data processing itself. *See SmartGene, Inc. v. Advanced Biological Labs., SA*, 555 F. App'x 950, 955 (Fed. Cir. 2014) (claim directed "the mental steps of comparing new and stored information and using rules to identify medical options" which was held to be unpatentable subject matter); *Elec. Power Grp., LLC v. Alstom*, 830 F.3d 1350, 1353–54 (Fed. Cir. 2016) (presenting the results of the collection and analysis without more are patent ineligible abstract concepts). Comparing detection signals based on different test environments by mathematically

calculating "quality metrics" thereon is the type of rule-based comparison with generation of options that was held abstract in *SmartGene*.

Appellants argue that the presence of affinity sensors (App. Br. 10), detection signals (App. Br. 11) and affinity binding to test sites (App. Br. 12) distinguishes the claimed invention from database systems such as those in *SmartGene*. However, the receiving and processing of data to detect binding signals, including data gathered from sources being monitored such as test sites on a microarray, is the type of routine data processing held abstract in *Elec. Power Group*, 830 F.3d at 1353, 1355.

Appellants assert that the rejection must rely on evidence, case law, or intrinsic evidence, and address the limitations individually and as a whole, and that the Examiner fails to do so. App. Br. 4–9. However, as above, the Examiner's Answer provided evidence explaining why the claims were abstract. *See* Ans. 2–7, 13. Further, there is no dispute that steps such as using test samples in different test environments and obtaining detection signals for quantification of molecules in these samples are well-understood, routine and conventional in diagnostic assays. *See* Spec. ¶ 3 ("affinity based sensors . . . are considered to be the state-of-the-art in detection of biomarkers"); Spec. ¶ 8 ("Various approaches to mitigate the errors encountered when using multiplexed measurement platforms have been developed including the provision of a coefficient of variation indicative of the consistency between various test sites on a platform"); Spec. ¶ 59 ("samples were then washed and read using an Axon Fluorescent scanner (commercially available from MDS Analytical Technologies, Sunnyvale, CA"); Spec. ¶ 28 ("processing circuit 104 may suitably be a general purpose

computer processing circuit such as a microprocessor and its associated circuitry.") Indeed, Appellants acknowledge that the use of multiple sample types exposed to the same environment represents a known approach (*see* App. Br. 14). Therefore, any novelty in the claimed invention solely resides in the application of the mathematical algorithm used for the quality metrics, and not in the manipulative steps of the method.

We are not persuaded by Appellants argument that "the claim does not monopolize an abstract idea. For example, the preamble of claim 1 limits the scope of claim. Claim 1 recites 'a confidence test for an assay'. Thus, not *all* confidence tests fall within the scope of the claim, only confidence tests of assays" (App. Br. 14). "While preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1379 (Fed. Cir. 2015). In this case, Appellants' attempt to limit the breadth of the claims by showing that other error mitigation techniques fall outside of the scope of the claims does not change the conclusion that the claims are directed to patent ineligible subject matter. Indeed, the open "comprising" nature of the claim does not exclude the use of other techniques. Moreover, where claims are deemed only to disclose patent ineligible subject matter under the *Mayo* and *Alice* framework, as they are in this case, preemption concerns are "fully addressed and made moot." *See Ariosa*, 788 F.3d at 1379.

We also are not persuaded by Appellants' argument that through the process of claim 1, the "controlled sample is thus 'transformed' into a metric

which represents a variation in the proportion of molecules of interest bound at each of the first and the second thermodynamic state" (App. Br. 19).

This "transformation" represents application of a mathematical relationship to signal data obtained from standard microarrays using standard detection systems and standard computers. *See* Spec. ¶ 31 citing US 5,807,522 for "a method for forming microarrays"; Spec. ¶ 59 for "Axon Fluorescent scanner"; and Spec. ¶ 28 for "a general purpose computer."

The Specification discloses mathematical formulas for determining a quality metric, teaching:

> An end point difference quality metric is determined using the following equation:
>
> $$Q_M = S_1(t_f) - S_2(t_f)$$
>
> wherein
>
> S_1 is the signal obtained from a test site at a first test environment,
>
> t_f is the final assay time after completion of the procedure 150, and
>
> S_2 is the signal obtained from a test site at a second test environment.

(Spec. ¶ 42). The Specification teaches additional quality metric equations for normalized rate of change Q_M (Spec. ¶ 44) and normalized log rate of change Q_M (Spec. ¶ 45).

Thus, the difference between the instant claim 1 and the prior art resides in the application of the mathematical analysis determining a quality metric based on the assay data, and not on the manipulative steps of the assay itself. This mathematical analysis is a way to apply an algorithm to information, here assay information comparing different detection signals,

and obtain a new form of data, a "confidence" value based on the organized information.

> This case is similar to *Digitech Image Technologies, LLC v. Electronics for Imaging, Inc.*, 758 F.3d 1344 (Fed. Cir. 2014). There, the claims of the challenged patent were directed to the abstract idea of organizing information through mathematical correlations. *Id.* at 1350–51. . . . A process that started with data, added an algorithm, and ended with a new form of data was directed to an abstract idea. *Id.*

RecogniCorp, LLC v. Nintendo Co., Ltd., 855 F.3d 1322, 1327 (Fed. Cir. 2017).

Because the claims are directed to an abstract idea/natural law, we turn to the second step of the *Alice* framework.

Alice Step Two

In *Alice* step two, we examine the elements of the claims to determine whether they contain an inventive concept sufficient to transform the claimed naturally occurring phenomena into a patent-eligible application. *Mayo*, 566 U.S. at 71–72 (quoting *Alice*, 134 S. Ct. at 2355). We must consider the elements of the claims both individually and as an ordered combination to determine whether additional elements transform the nature of the claims into a patent-eligible concept. *Ariosa*, 788 F.3d at 1375.

The Specification acknowledges that "multiplexed measurement platforms such as protein arrays are a promising diagnostic technology that are currently being explored in conducting the diagnostic tests" (Spec. ¶ 3). The Specification further acknowledges that "[s]uch multiplexed measurement platforms frequently incorporate affinity based sensors which are considered to be the state-of-the-art in detection of biomarkers" (*id.*).

The Specification recognizes these platforms as prior art, teaching that the procedures may "be used in a variety of test site platforms including 96-well plates, plates with fewer or additional wells, microarray platforms, printed circuit board platforms, CMOS chip platforms, multiplexed assays, protein arrays, lateral flow devices, sandwich assays, competitive assays, bead based arrays, or other appropriate platforms" (Spec. ¶ 65).

The Specification teaches, regarding first "exposing" manipulative step, the known diagnostic analysis of uncontrolled samples including "human body fluids such as blood, serum, saliva, biological cells, urine, or other biomolecules" and "consumables such as milk, baby food, or water" (Spec. ¶ 2).

Pi, cited by the Examiner in the obviousness rejection, evidences that the use of multiple measurements to normalize signals from each image spot on a microarray was a known approach (Pi 21:17–36). Pi also evidences that the test environment must be analyzed, including environmental factors such as temperature, to provide reference signals for comparison with the test samples that relate to the environmental factors (*see* Pi 9:27–33).

The Specification teaches, regarding the signal detection step, the use of known sensors where "the sensors incorporated into the environment detector suite 114 may include IR sensors, and Hall sensors. AMR sensors or GMR sensors may be provided to monitor the density of magnetic beads on a test site surface. ISFETs or CMOS based charge detection circuits may be used in electrochemical embodiments" (Spec. ¶ 64).

Lastly, the Specification teaches, regarding the "determining quality metric" and "confidence test" that "the processing circuit 104 executes the

program instructions 108 to execute at least some of the procedure 250" (Spec. ¶ 53) and the "processing circuit 104 may suitably be a general purpose computer processing circuit such as a microprocessor and its associated circuitry" (Spec. ¶ 28).

The Examiner finds the

> additional steps do not reflect any technological improvement to any experiment, test, or measurement technique, rather they delineate only the most generic description of steps that must be practiced in order to obtain a first and second "quality metric" and the abstract mental steps encompassing the appreciation of a practitioner with respect to any measurable differences between "a first and second quality metric."

(Ans. 7).

In sum, the evidence of record supports the Examiner's position that the claims do not add something "significantly more" to the abstract idea and/or law of nature. Instead, each of the steps in the "claims (e.g., arranging, storing, retrieving, sorting, eliminating, determining) are conventional, routine, and well-known." *Versata Development Group, Inc. v. SAP Am., Inc.*, 793 F.3d 1306, 1335 (Fed. Cir. 2015). The Federal Circuit decided

> [i]n order for the addition of a machine to impose a meaningful limit on the scope of a claim, it must play a significant part in permitting the claimed method to be performed, rather than function solely as an obvious mechanism for permitting a solution to be achieved more quickly, i.e., through the utilization of a computer for performing calculations.

SiRF Tech., Inc. v. Int'l Trade Comm'n, 601 F.3d 1319, 1333 (Fed. Cir. 2010).

We conclude that the practice of the method claims does not result in an inventive concept that transforms the abstract idea/natural phenomena of performing mathematical quality metrics on biological assay data to obtain confidence tests into a patentable invention. *Mayo* and *Ariosa* make clear that transforming claims that are directed to an abstract idea or law of nature requires more than simply stating the abstract idea or law of nature while adding the words "apply it." *Mayo*, 566 U.S. at 72; *Ariosa*, 788 F.3d at 1377.

We find Appellants' reliance on *Rapid Litigation Management Ltd. V. CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. 2016) unpersuasive (*see* Reply Br. 2, 5–6). *Rapid Litigation* found the "end result of the '929 patent claims is not simply an observation or detection of the ability of hepatocytes to survive multiple freeze-thaw cycles. Rather, the claims are directed to a new and useful method of preserving hepatocyte cells." *Id.* at 1048. That is, the distinction in *Rapid Litigation* was that while detecting or observing the cells was an abstract idea, the method of preserving cells was not. *Rapid Litigation* does not suggest that the present claims, which are entirely drawn to detecting or observing microarrays and then mathematically transforming the data using quality metrics to form a confidence test, are patentable because the addition of the mathematical formulae "simply changes the data into other forms of data [that] cannot save [the claims]." *RecogniCorp*, 855 F.3d at 1328.

We also find Appellants' reliance on *Amdocs (Israel) Limited v. Openet Telecom, Inc.*, 841 F.3d 1288 (Fed. Cir. 2016) unavailing. (Reply Br. 3–4, 6–10). The claims in *Amdocs* were drawn to improvements in the

operation of a computer itself at a task, rather than applying a computer and mathematical equation to analyze data from known assays. *See Amdocs*, 841 F.3d at 1301. Indeed, *Amdocs* notes prior ineligible claims were "not tied to any particularized structure, broadly preempted related technologies, and merely involved combining data in an ordinary manner without any inventive concept." *Id.* That is the current case, where instant claim 1 is not tied to any particularized structure and combines data in an ordinary manner based on a disclosed algorithm. Therefore, *Amdocs* does not persuade us that Appellants' claims relying on quality metrics and confidence tests using known computer components and known prior art mathematical algorithms as discussed above are patentable subject matter.

We therefore conclude that Supreme Court and Federal Circuit precedent constrains us to conclude that all of the claims on appeal are directed to patent-ineligible subject matter.

B. 35 U.S.C. § 103(a) over Pi

The issue with respect to obviousness is: Does the evidence of record support the Examiner's conclusion that Pi renders the claims obvious?

Findings of Fact

1. Pi teaches "reference steps can be used to provide optical reference signals under illumination of probe light and the optical reference signals can be used correct certain inaccuracies or errors in measurement, e.g., inaccuracies or errors caused by instrumentation drift, liquid properties changes, or environmental factors (for example temperature change)" (Pi 9:27–33).

2. Figure 2C of Pi is reproduced below:

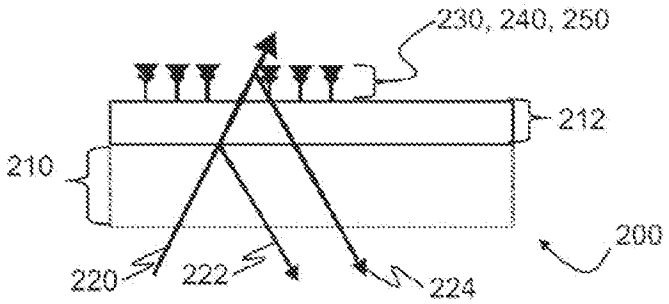

FIG. 2C

FIG. **2**C is a cross sectional view of the biochip **200** having sample biomolecules **250** interacting with reagents **240** at the reagent immobilizing site **230**. The first reflected beam **222** is reflected off the boundary between the substrate **210** and the thin-film layer **212** . . . . The second reflected beam **224** reflected off the reagent immobilizing site **230** is changed by the interactions between the sample biomolecules **250** and the immobilized reagents **240**. This change in the light path of the second reflected beam **224** is calculated as height increases due to the molecular interactions between the sample biomolecules **250** and the reagents **240** at the reagent immobilizing sites **230**.

(Pi 12:30–41).

3. Pi teaches:

The label-free biochip contains reagent immobilizing sites for immobilizing reagents, such as antibodies. Before immobilizing the reagents, an initial measurement provides a baseline image dataset of a blank (no reagents immobilized) biochip. Then, the reagent immobilizing sites on the substrate can be treated with different methods (e.g., surface chemistry) to activate the surfaces of the reagent immobilizing sites for immobilizing reagents. A second measurement can be performed to determine the effect, if any, of the surface activation on substrate thickness. Reagent molecules of choice (e.g., antibodies) are applied to the reagent immobilizing sites to locally immobilize the reagents. A third measurement can be performed to determine the effect of the immobilized reagents

> on the substrate thickness. After the effect of the immobilized reagents is measured, a simple solution of target biomolecules can be added to the reagent immobilizing sites to detect molecular interactions. For example, conventional Enzyme-Linked ImmunoSorbent Assay (ELISA) techniques or other convention molecular interaction detection techniques (with different label read-out) can be implemented to detect captured molecules. A fourth measurement can be performed to detect molecular interactions based on localized changes in the substrate thickness. The first three measurements can be used to normalize ELISA signals from each image spot, and thus more precise measurements can be accomplished.

(Pi 21:11–36).

Principles of Law

A prima facie case for obviousness "requires a suggestion of all limitations in a claim," *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

Analysis

Appellants contend "claim 1 requires the *binding* of the molecules to occur at two different thermodynamic states. A molecule *existing* in two different thermodynamic states is not the same as *binding* molecules *at* two different thermodynamic states" (App. Br. 23). Appellants contend "the simple existence of bound molecules 250 in FIG. 2C cannot indicate a variation in a proportion of the molecules of interest in the control sample that are bound" (App. Br. 24). Appellants contend "[t]herefore, Pi fails to disclose a quality metric for the molecule of interest indicative of a variation

in a proportion of the molecules of interest in the control sample that are bound" (*id.*). Appellants also contend that column 21 of Pi "fails to expressly describe a second quality metric for the molecule of interest indicative of a variation in a proportion of the molecules of interest in the uncontrolled sample that are bound" (App. Br. 26).

The Examiner responds "Appellant is taking the position that the claims must be interpreted narrowly and in a privileged manner so as to import limitations and preferred embodiments from the instant disclosure into the claims. The examiner however applies a broadest reasonable interpretation standard" (Ans. 14).

We find that Appellants have the better position. While we agree with the Examiner that it is "during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed." *In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989), claim 1 broadly requires two different quality metrics be determined for binding at two different thermodynamic states. Even if we agreed with the Examiner that ELISA analysis at column 21 of Pi represents binding at two different thermodynamic states, based on different surface chemistries or antibodies, there is no indication, teaching, or suggestion in Pi that two different quality metrics are calculated using this binding data (FF 3). Nor does the Examiner provide a reason to apply first and second quality metrics as required by claim 1 to the disclosure of Pi (FF 1–3). We therefore agree with Appellants that "Pi fails to disclose a second quality metric for the molecule of interest indicative of a variation in a proportion of the

molecules of interest in the uncontrolled sample that are bound" (App. Br. 27) and therefore does not render claim 1 obvious.

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that Pi renders the claims obvious.

SUMMARY

In summary, we affirm the rejection of claims 1–13 and 23 under 35 U.S.C. § 101 as being directed to non-statutory subject matter.

We reverse the rejection of claims 1–13 and 23 under 35 U.S.C. § 103(a) as obvious over Pi.

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