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General Electric Company
GE Global Patent Operation
901 Main Avenue
3rd Floor
Norwalk, CT 06851
UNITED STATES OF AMERICA

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BORIN, MICHAEL L	

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KARL ANDERSSON

Appeal 2017-007312
Application 14/000,431
Technology Center 1600

Before RICHARD M. LEBOVITZ, JEFFREY N. FREDMAN, and RICHARD J. SMITH, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1,2] under 35 U.S.C. § 134 involving claims to a method of screening a plurality of fluid samples for the presence of analytes capable of specifically binding to a ligand immobilized on a sensing surface of a sensor. The Examiner rejected the claims as directed to non-statutory subject matter and as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm the non-statutory subject matter rejection but reverse the obviousness rejections.

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[1] Appellant identifies the Real Party in Interest as GE Healthcare Bio-Sciences AB (App. Br. 2).

[2] We have considered and herein refer to the Specification of Aug. 20, 2013 ("Spec."); Final Office Action of July 8, 2016 ("Final Action"); Appeal Brief of Nov. 28, 2016 ("App. Br."); Examiner's Answer of Feb. 10, 2017 ("Answer") and Reply Brief of Apr. 10, 2017 (Reply Br.).

Statement of the Case

Background

"Optical biosensors based on surface plasmon resonance (SPR) are today widely used for analyzing a wide range of biological and chemical interactions. SPR biosensors allow the determination of the affinity and kinetics of molecular interactions in real time without the need for a molecular tag or label" (Spec. ¶ 2). SPR binding data are typically "first subjected to a number of signal correction adjustments, including at least some of molecular weight adjustment to compensate response values for different analyte sizes, bulk refractive index surface errors, adjustment for decreasing activity of the immobilized ligand (protein), and capture level adjustment when different ligands are used" (Spec. ¶ 4). "A binding level against cycle number (i.e. sample no.) is plotted and a binding level limit (or sometimes more than one limit) is then selected by the user" (*id.*). All "samples (analytes) exhibiting a binding level above the selected limit" are "considered as more or less strong binders" (*id.*). "While this procedure is simple and in several respects gives comprehensible results, the user risks missing true binders which for some reason do not reach the correct level" (Spec. ¶ 5). "A more sophisticated screening evaluation method which identifies all true binders would therefore be desired" (Spec. ¶ 6). "The above-mentioned object as well as other objects and advantages are achieved by an evaluation method based on a multiparametric analysis of the response curves, or binding curves, rather than merely measurement of binding levels therefrom" (Spec. ¶ 7).

The Claims

Claims 1–11 are on appeal. Claim 1 is representative and reads as follows:

> 1. A method of screening a plurality of fluid samples for the presence of analytes capable of specifically binding to a ligand immobilized on a sensing surface of a sensor, the method comprising:
>
> passing a plurality of fluid samples having an analyte over a biosensor sensing surface, wherein the analyte of each fluid sample interacts with a ligand immobilized on the biosensor sensing surface;
>
> producing response curves representing the progress of each interaction over time;
>
> subjecting a set of the response curves to a multiparametric evaluation procedure, the evaluation procedure comprising:
>
> determining for each response curve a binder classification based on at least two binding-related features of the response curve,
>
> identifying response curves for which the binder classification deviates significantly from that of the remaining response curves as a group, and
>
> classifying these deviating response curves as representing sample analytes which are binding partners to the ligand; and
>
> identifying to a user the sample analytes which are binding partners to the ligand.

The Rejections

A. The Examiner rejected claims 1–11 under 35 U.S.C. § 101 as directed to non-statutory subject matter (Ans. 2–4).

B. The Examiner rejected claims 1–9 and 11 under 35 U.S.C. 103(a) as being obvious over Andersson[3] in view of Fowler[4] and Karlsson[5] (Ans. 5–9).

C. The Examiner rejected claim 10 under 35 U.S.C. 103(a) as being obvious over Andersson in view of Fowler, Karlsson, and Steinthal[6] (Ans. 10).

A. 35 U.S.C. § 101

The Examiner finds that the claims on appeal are directed to patent-ineligible subject matter. Specifically, the Examiner finds that the claims are directed to "an abstract idea" (Ans. 3). The Examiner finds that the claims "are directed to . . . processing information, converting one form of numerical representation into another, and comparing information. All of these concepts relate to organization and processing information (comparison of data) which can be performed mentally and is an idea of itself" (Ans. 3).

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[3] Andersson et al., US 8,155,906 B2, published Apr. 10, 2012.
[4] Fowler et al., *In Vitro Evaluation of Reversible and Irreversible Cytochrome P450 Inhibition: Current Status on Methodologies and their Utility for Predicting Drug-Drug Interactions*, 10(2) AAPS J., 410–24(1992).
[5] Karlsson et al., US 8,321,152 B2, published Nov. 27, 2012.
[6] Steinthal et al., US 7,171,312, published January 30, 2007.

The Examiner also finds that although the claim recites "the additional limitation of passing fluid samples having analyte over a biosensor sensing surface", this step is well understood, routine, and conventional (Ans. 3).

The Examiner reached these conclusions by applying the test set out in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012) (Ans. 2–4) based on the two-step *Alice* framework. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014).

Appellant contends that the claims are not directed to an abstract idea, that the claims do not preempt all uses of the abstract idea, and that the claims include additional elements or something more that transforms the nature of the claims into a patent-eligible application (App. Br. 4–13).

Analysis

To determine whether a claim is invalid under § 101, we employ the two-step *Alice* framework. In *Alice* 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 patent ineligible concepts. *Ariosa*, 788 F.3d at 1376. 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).

Alice Step One

Claim 1 is directed to an abstract idea. In particular, the recited steps of

> producing response curves representing the progress of each interaction over time; subjecting a set of the response curves to a multiparametric evaluation procedure, the evaluation procedure comprising: determining for each response curve a binder classification based on at least two binding-related features of the response curve, identifying response curves for which the binder classification deviates significantly from that of the remaining response curves as a group, and classifying these deviating response curves as representing sample analytes which are binding partners to the ligand; and identifying to a user the sample analytes which are binding partners to the ligand

all involve categorizing and/or analyzing information.

> Information as such is an intangible . . . . Accordingly, we have treated collecting information, including when limited to particular content (which does not change its character as information), as within the realm of abstract ideas . . . . In a similar vein, we have treated analyzing information by steps people go through in their minds, or by mathematical algorithms, without more, as essentially mental processes within the abstract-idea category

Electric Power Group, LLC v. Alstom S.A., 830 F.3d 1350, 1353–54 (Fed. Cir. 2016) (internal citations omitted)). Additionally, the Federal Circuit in *Electric Power Group* stated that the "advance they purport to make is a process of gathering and analyzing information of a specified content, then displaying the results, and not any particular assertedly inventive technology for performing those functions" (*id.* at 1354). Here, Appellant admits the

advancement is the process of analyzing information. Specifically, Appellant admits:

> Appellant discovered a particular solution to this problem—using multiparametric analysis of binding curves that includes determining at least two binding-related features of each response curve and, assuming that the majority of screened analytes are non-binders or bad binders, identifying outliers (i.e. binding curves whose binder classification deviates the most from the average binder classification of all the curves) as true binders—and the claims set forth the specific series of steps that implement this solution.

(App. Br. 8).

In *Digitech*, the Federal Circuit stated that "[w]ithout additional limitations, a process that employs mathematical algorithms to manipulate existing information to generate additional information is not patent eligible. 'If a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory'" *Digitech Image Technologies, LLC v. Electronics for Imaging, Inc.*, 758 F.3d 1344, 1351 (Fed. Cir. 2014). Here, the process employs mathematical algorithms to manipulate existing information to generate additional information and therefore is not patent eligible.

Moreover, the producing and selecting steps are the type of work that can be performed mentally and therefore are abstract ideas. As the Federal Circuit explained, "methods which can be performed mentally, or which are the equivalent of human mental work, are unpatentable abstract ideas--the 'basic tools of scientific and technological work' that are open to all'"

CyberSource Corp. v. Retail Decisions, Inc., 654 F.3d 1366, 1371, (Fed. Cir. 2011) (*citing Gottschalk v. Benson*, 409 U.S. 63, 175 USPQ 673 (1972)).

This case is distinguishable, for example, from cases like *Diamond v. Diehr*, 450 U.S. 175 (1981), because in *Diehr*, an algorithm was used to control the change in state of rubber in a curing process. *In re Diehr*, 602 F.2d 982, 983–84 (CCPA 1979). The algorithm calculated the Arrhenius equation for the reaction time during the cure to determine when the compound was cured and to automatically open the press when the cured state was achieved. *Id.* In the rejected claims, the recited algorithm is not used to determine when a change of state is complete as it was in *Diehr*. Rather, in the rejected claims, the algorithm is utilized to analyze data obtained by a fluid samples, but no final physical step analogous to opening the press after curing is present. Instead, the final "identifying" clauses in the instant claims "tell the relevant audience about the laws while trusting them to use those laws appropriately where they are relevant to their decisionmaking." *Mayo*, 566 U.S. at 78. Thus, the algorithm does not tell when the change of state is complete and to perform a manipulative step based on it as in *Diehr*.

Because the claims are directed to an abstract idea, 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 abstract idea 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 the additional elements transform the nature of the claims into a patent-eligible concept. *Ariosa*, 788 F.3d at 1375.

The Specification acknowledges that "[o]ptical biosensors based on surface plasmon resonance (SPR) are today widely used for analyzing a wide range of biological and chemical interactions" (Spec. ¶ 2). The Specification also acknowledges that

> **A typical screening procedure, wherein a plurality of fluid samples are tested for the presence of species capable of specifically binding to a desired receptor or ligand comprises contacting each sample with a sensing surface supporting the receptor or ligand and usually also a reference surface without immobilized receptor or ligand, measuring the responses at the surfaces, and evaluating the measurement data including subtracting the response at the reference surface from that at the sensing surface**. Typically, the binding data obtained are first subjected to a number of signal correction adjustments, including at least some of molecular weight adjustment to compensate response values for different analyte sizes, bulk refractive index surface errors, adjustment for decreasing activity of the immobilized ligand (protein), and capture level adjustment when different ligands are used. A binding level against cycle number (i.e. sample no.) is plotted and a binding level limit (or sometimes more than one limit) is then selected by the user, all samples (analytes) exhibiting a binding level above the selected limit being considered as more or less strong binders

(Spec. ¶¶3–4) (emphasis added).

Thus, the Specification acknowledges that SPR is routine and conventional ("widely used") and that the step of passing a plurality of fluid samples having an analyte over a biosensor sensing surface, wherein the analyte of each fluid sample interacts with a ligand immobilized on the biosensor sensing surface is also routine and conventional. Moreover,

Karlsson teaches "biosensors and affinity analysis are known per se in the art" (Karlsson 3:17–18). Karlsson also teaches the step of passing a plurality of fluid samples having an analyte over a biosensor sensing surface, wherein the analyte of each fluid sample interacts with a ligand immobilized on the biosensor sensing surface, thereby indicating that such steps are routine and conventional (Karlsson 4:27–55). Similarly, Andersson teaches that surface plasmon resonance devices were commercially available in the prior art, teaching a "representative biosensor system is the Biacore® instrumentation sold by Biacore AB (Uppsala, Sweden) which uses surface plasmon resonance (SPR) for detecting interactions between molecules in a sample and molecular structures immobilized on a sensing surface" (Andersson 1:30–34).

In sum, the evidence of record supports the Examiner's position that the claims do not add something "significantly more" to the abstract idea. Instead, the evidence shows that the additional elements in the claims (e.g., passing a plurality of fluid samples having an analyte over a biosensor sensing surface, wherein the analyte of each fluid sample interacts with a ligand immobilized on the biosensor sensing surface) are conventional, routine, and well-known. We conclude that the method claim does not result in an inventive concept that transforms the abstract idea described above into a patentable invention.

Appellant contends that the "Examiner's determination that the claims are directed to 'processing information, converting one form of numerical representation into another, and comparing information' is divorced from the claim language itself and violates the Federal Circuit's express instructions to avoid oversimplifying the claims" and "eviscerates numerous, specific

limitations throughout the claims" (App. Br. 6). Appellant further argues the "overbreadth of the Examiner's characterization is readily apparent from the myriad of activities that could be described as processing information, converting numbers, and comparing information but which are plainly not captured by Appellant's claims" (App. Br. 7). Appellant contends the "focus of the claims, when read in light of the specification, is on a specific method of screening a pool of molecular species to determine their capability of binding to a desired receptor or ligand" (App. Br. 7).

We find these arguments unpersuasive because the producing and subjecting steps are directed to an abstract mathematical approach to data analysis that is applied to the particular known test format of analytical biosensor systems, not to any improvement in the analytical biosensor itself. "'If a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory.'" *Digitech Image Technologies, LLC v. Electronics for Imaging, Inc.*, 758 F.3d 1344, 1351 (Fed. Cir. 2014).

Similar to the claims in *Electric Power Group*, these steps are directed to data analysis and mathematical calculations, because they transform the data to another form without applying the resulting data further to the method to alter anything other than data. That is, the analysis of the response curves of the biosensor does not change anything about how the biosensor itself operates, nor is anything physical in the biosensor altered by the claimed method. Rather the instant claims focus on particular mathematical operations for analysis of the biosensor data, whether multiparametric evaluation or the more specific analysis of response curves, "is on selecting certain information, analyzing it using mathematical

techniques, and reporting or displaying the results of the analysis. That is all abstract." *SAP America, Inc. v. Investpic, LLC*, 898 F.3d 1161, 2018 WL 3656048 *5 (Fed. Cir. 2018).

Appellant contends "prior to Appellant's work, there was a need for a more sophisticated screening evaluation method that identifies more or all true binding analytes. Appellant discovered a particular solution to this problem—using a multiparametric analysis of binding curves that includes determining at least two binding-related features of each response curve" (App. Br. 8).

We do not dispute that the use of mathematical operations in this case may be "a positive and valuable contribution to science. But even such valuable contributions can fall short of statutory patentable subject matter, as it does here." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1380 (Fed. Cir. 2015). We note that even the limitation to the particular biosensor environment does not rescue the claim from being abstract because "limitation of the claims to a particular field of information . . . does not move the claims out of the realm of abstract ideas." *SAP*, 2018 WL 3656048 *6.

Appellant argues that the claims do not preempt processing information, converting numbers and comparing information (App. Br. 9–10). While preemption is the concern underlying the judicial exceptions, it is not a stand-alone test for determining eligibility. *Rapid Litig. Mgmt. v. CellzDirect, Inc.,* 827 F.3d 1042, 1052, (Fed. Cir. 2016). "[W]e have consistently held that claims that are otherwise directed to patent-ineligible subject matter cannot be saved by arguing the absence of complete

preemption." *Return Mail, Inc. v. United States Postal Service*, 868 F.3d 1350, 1370 (Fed. Cir. 2017).

Appellant contends "even if the claims were directed to a judicial exception, which they are not, they certainly claim an inventive concept that amounts to significantly more than the alleged judicial exception" (App. Br. 10). Appellant contends the "inventive concept rests on conducting a multiparametric analysis of binding curves that includes determining at least two binding-related features of each response curve, and subsequently identifying outliers as true binders." (App. Br. 11). Appellant contends the "Examiner has failed to establish that the claimed subject matter does not amount to significantly more than the alleged judicial exception" (App. Br. 12).

We find these arguments unpersuasive because, as Appellant acknowledges even in the argument, the inventive concept is drawn to the mathematical analysis by "multiparametric evaluation" (*see* App. Br. 8) and not to something sufficient to transform this abstract idea into a patent-eligible application. We find Appellant's reliance on *Amdocs (Israel) Limited v. Openet Telecom, Inc.*, 841 F.3d 1288 (Fed. Cir. 2016) unavailing (*see* App. Br. 11). 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 novel or unobvious structure for a biosensor as evidenced by

Karlsson and Andersson as discussed above. Instead, claim 1 uses standard biosensors and biosensor data with a multiparametric evaluation algorithm that does not improve operation of the biosensor itself, but rather improves analysis of data generated by the biosensor.

We also find Appellant's reliance on *McRO, Inc. v. Bandai Namco Games America Inc.*, 837 F.3d 1299 (Fed. Cir. 2016) unavailing (see App. Br. 12–13). The claims in *McRO* were drawn to improvements in the operation of a computer itself at a task of lip reading, rather than applying a computer to perform known tasks. *See McRO*, 837 F.3d at 1314. Here, Appellant has not demonstrated an improvement in the operation of the computer itself, but at best suggests an improvement in the application of a multiparametric analysis algorithm for characterization of biosensor data.

Therefore, neither *Amdocs* nor *McRO* persuades us that Appellant's claims relying on multiparametric evaluation using known biosensor components as discussed above are patentable subject matter that provide something "significantly more."

We therefore conclude that all of the claims on appeal are directed to patent-ineligible subject matter.

B. and C. 35 U.S.C. 103(a)

Because both of these rejections rely upon the combination of Andersson, Fowler, and Karlsson, we will consider them together.

The Examiner finds Andersson teaches screening of fluid samples as required by claim 1 but "does not teach that a binder classification that deviates from the group represents presence of a binding analyte" (Ans. 7).

The Examiner relies on Fowler to teach "that curves viewed as 'outliers' reflect different character of binding such as binding to more regions of active site" (Ans. 7). The Examiner finds it obvious "to select, as a result-oriented variable, the descriptors that reflect binding, and to expect that carrying out the analysis using binding-related descriptors will be as successful as using quality-related descriptors in Andersson" (Final Act. 9).

Findings of Fact

1. Andersson teaches:

> A method of analysis, comprising
> A) detecting molecular binding interactions between analytes in a sample and molecular structures immobilized on one or more sensing surface areas of a biosensor;
> B) producing a plurality of binding response curves to form a resulting set, each response curve representing a binding interaction of an analyte with a molecular structure over time, each response curve comprising an analyte association part and an analyte dissociation part;
> C) subjecting the resulting set of response curves to a data-processing procedure for assessment of a quality of each of the response curves with respect to a presence of oddities in the response curves the subjecting operation comprising the substeps of:
> 1) selecting at least two quality-related parameters for the response curves, each of the parameters defining a quality descriptor;
> 2) computing for each response curve, values for the quality descriptors, which represent the quality of the response curve;
> 3) based on the values for the quality descriptors, classifying the response curves by computing for each response curve a quality classification which indicates a deviation of the quality descriptors of the corresponding response curve from the quality descriptors of the other response curves in the resulting set produced in the producing operation;

> 4) selecting a predetermined number of the response curves having quality classifications corresponding to the largest deviations, and defining the predetermined number of response curves as odd quality response curves;
> 5) displaying the odd quality response curves to a user of the biosensor for visual inspection thereof to thereby decide if an odd quality response curve should be used in the analysis or be rejected;
> 6) removing odd quality response curves rejected by the user;
> 7) repeating steps 3) to 6) until no more of the odd quality curves are rejected; and
> 8) determining from the remaining response curves at least one of molecular surface concentrations and kinetic parameters.

(Andersson 14:43 to 15:57, claim 1).

2. Karlsson teaches passing a plurality of fluid samples having an analyte over a biosensor sensing surface, wherein the analyte of each fluid sample interacts with a ligand immobilized on the biosensor sensing surface; (Karlsson 4:27–60).

3. Fowler teaches that diferent binding sites have different characteristics (Fowler 420–421).

Principles of Law

The test for analogous art is "(1) whether the art is from the same field of endeavor, regardless of the problem addressed and, (2) if the reference is not within the field of the inventor's endeavor, whether the reference still is reasonably pertinent to the particular problem with which the inventor is involved." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004).

Analysis

Appellant contends that Fowler is not analogous art, because "Fowler is in a different field of endeavor as the current invention and relates to a problem different from the one faced by the inventors of the current invention" (Reply Br. 4).

We agree with Appellant. The Examiner has not established that Fowler is in the same field of endeavor as the current invention or is reasonably pertinent to the problem faced by the inventor. Moreover, the Examiner has not established that one would look to Fowler in order to distinguish ligand binding through analyzing binding curves. Thus, the Examiner has not established that Fowler is properly analogous art pertinent to the problems with which the inventor would have been concerned.

We also agree with Appellant that the Examiner did not provide persuasive reasoning based on "Andersson and/or Karlsson that would have led one of ordinary skill to modify or to combine Fowler with Andersson and/or Karlsson to arrive at the claimed invention" (Reply Br. 6).

Conclusion of Law

The evidence of record does not support the Examiner's conclusion that the combination of Andersson, Fowler, and Karlsson renders the claims obvious.

SUMMARY

In summary, we affirm the rejection of claim 1 under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Pursuant to 37 C.F.R. § 41.37(c)(1), we also affirm the rejection of claims 2–11 as being directed to non-statutory subject matter as these claims were not argued separately.

We reverse the rejection of claims 1–9 and 11 under 35 U.S.C. § 103(a) as obvious over Andersson, Fowler, and Karlsson.

We reverse the rejection of claim 10 under 35 U.S.C. 103(a) as being obvious over Andersson, Fowler, Karlsson, and Steinthal.

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