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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte RICHARD P. VAN DUYNE, MATTHEW R. GLUCKSBERG, JOSEPH T. WALSH JR., JONATHAN M. YUEN, and NILAM C. SHAH[1]

Appeal 2017-009873
Application 13/303,815
Technology Center 3700

Before ERIC B. GRIMES, JOHN G. NEW, and TIMOTHY G. MAJORS, *Administrative Patent Judges.*

NEW, *Administrative Patent Judge.*

DECISION ON APPEAL

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[1] Appellants identify Northwestern University as the real party-in-interest. App. Br. 3.

SUMMARY

Appellants file this appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 1–20 as unpatentable under 35 U.S.C. § 101 as being directed to nonstatutory subject matter.

Claims 1–20 also stand rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of Van Duyne et al. (US 2009/0118605 A1, May 7, 2009) ("Van Duyne") and Mahadevan-Jansen et al. (US 2010/0145200 A1, June 10, 2010) ("Mahadevan-Jansen").

Claims 1–20 stand further rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of Van Duyne et al. (US 2009/0118605 A1, May 7, 2009) ("Van Duyne") and Morris et al. (US 2009/0219523 A1, Sept. 3, 2009) ("Morris").

Claims 1–20 also stand rejected as unpatentable under the nonstatutory doctrine of obviousness-type double patenting over claims 1, 2, and 4 of US 8,592,226 B2 (Nov. 26, 2013) ("the '226 patent") and Morris.

We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

NATURE OF THE CLAIMED INVENTION

Appellants' invention is directed to systems and methods employing a surface-enhanced Raman biosensor and sensing devices for collecting spatially offset Raman spectra from the biosensor. Abstract.

REPRESENTATIVE CLAIM

Claim 1 is representative of the claims on appeal and recites:

> 1. A method for quantification of an analyte *in vivo*, comprising:
>
> a) acquiring, through the skin of a subject, a spatially offset Raman spectrum from a biosensor implanted under the skin of said subject, wherein said biosensor comprises a plurality of nanospheres and a metal film over said nanospheres; and
>
> b) quantifying the concentration of an analyte in said subject based on said spatially offset Raman spectrum.

App. Br. 14.

ISSUES AND ANALYSES

A. Rejection of claims 1–20 under 35 U.S.C. § 101

Issue

Appellants argue that the Examiner erred in concluding that the claims are unpatentable as being drawn to a judicially-created exception to 35 U.S.C. § 101, *viz.*, an abstract idea. App. Br. 12.

Analysis

The Examiner concludes that Appellants' claims 1–20 are directed to the abstract idea of quantifying the concentration of an analyte based on spatially offset Raman spectrum. Final Act. 3. The Examiner also finds that the claims do not include additional elements that are sufficient to amount to significantly more than the judicial exception, because the additional elements, such as biosensor and processor, are recited at a high level of generality, and provide conventional data collection elements and/or computer components performing functions that do not add meaningful limits to practicing the abstract idea. *Id.* The Examiner concludes

that the claims are directed to an abstract idea because, although not drawn to the same subject matter, these claim limitations are similar to mathematical concepts and operations for manipulating and/or relating data, organizing information through correlations, and/or collecting and comparing known data, and thus constitute an abstract idea. *Id.*

Appellants argue that limitation reciting: "acquiring, through the skin of a subject, a spatially offset Raman spectrum from a biosensor implanted under the skin of said subject, wherein said biosensor comprises a plurality of nanospheres and a metal film over said nanospheres" is a concrete (i.e., not abstract) step which represents significantly more than the quantifying step alone. App. Br. 12. Appellants assert that claim 2 further clarifies the concrete nature of the acquiring step by reciting "wherein said acquiring step comprises the steps of: (1) illuminating said biosensor at least one first spot with light; (2) collecting Raman scattering light from said biosensor at a [sic] at least one second spot [[spots]] in response to illumination by said light, wherein each second spot is apart from the at least one first spot so as to define a source-detection (S-D) offset distance." Appellants contend that the acquiring step is not merely an abstract idea, but a concrete step that must be performed. *Id.*

Appellants argue further that the claimed use of an implanted biosensor with the detection of spatially offset Raman spectrum had not been performed prior to the work conducted during development of the presently claimed invention. App. Br. 13. According to Appellants, it was accepted in the field that Surface-enhanced Raman spectroscopy ("SERS") and spatially offset Raman spectroscopy ("SORS") were incompatible, and that tools (mathematical or otherwise) were not available at the time of the invention to demonstrate otherwise.

Id. (citing Declaration of Richard P. Van Duyne[2], March 14, 2016 (the "Van Duyne Declaration") ¶¶ 4, 8). Appellants argue that the recited "acquiring" step utilizes a procedure that was not routine or conventional at the time of the invention; rather, the combination of SERS and SORS into a single method had never been performed prior to the present work, as is evident from the absence in the Examiner's search of any reference that teaches or suggests such a technique. *Id.*

The Examiner responds that the abstract idea of the claim consists of quantifying the concentration of an analyte based on a spatially offset Raman spectrum. Ans. 15. The Examiner finds that Appellants' Specification indicates SERS and SORS components and functions are well-understood, routine and conventional activity and, therefore, do not add significantly more to the abstract idea recited in the claims. *Id.*

We are not persuaded by the Examiner's reasoning. We agree with Appellants that the claims are directed to a method, i.e., a "process" and therefore fall into one of the broad statutory categories of patent-eligible subject matter under 35 U.S.C. § 101. We consequently next turn to determine whether this process is patent eligible or comes under one of the nonstatutory exceptions to Section 101.

In performing such a patentability analysis under 35 U.S.C. § 101, we follow the framework set forth by the Supreme Court in *Mayo Collaborative Servcs. v.*

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[2] Dr. Richard P. Van Duyne, one of the named inventors of the instant application, is Charles E. and Emma H. Morrison Professor of Chemistry at Northwestern University, the author of over 300 peer-reviewed publications, and the discoverer of Surface-enhanced Raman Spectroscopy ("SERS"). Van Duyne Declaration ¶ 2. We find Dr. Van Duyne sufficiently qualified to render an expert opinion in this appeal.

Prometheus Labs. Inc., 566 U.S. 66 (2012). As a first step, we determine whether the claims at issue are directed to a patent-ineligible concept, i.e., a law of nature, a phenomenon of nature, or an abstract idea. *Mayo*, 566 U.S. at 70–71. If the claims are so directed, we next consider the elements of each claim both individually and "as an ordered combination" to determine whether additional elements "transform the nature of the claim" into a patent-eligible application. *Id.* at 78–79; *see also Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015).

Specifically, the Supreme Court considered this second step as determining whether the claims recite an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Mayo*, 566 U.S. at 72–73.

We agree with the Examiner that the limitation reciting: "quantifying the concentration of an analyte in said subject based on said spatially offset Raman spectrum" recites an abstract idea – a quantification of an analyte based upon an observed spectrum. However, all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas. *Mayo*, 566 U.S. at 71. We, therefore turn to the remaining limitations to determine whether they add significantly more to the abstract idea itself. *Id.* at 72–73.

We conclude that they do. Claim 1 recites: "acquiring, through the skin of a subject, a spatially offset Raman spectrum from a biosensor implanted under the skin of said subject, wherein said biosensor comprises a plurality of nanospheres and a metal film over said nanospheres." As Appellants explain, combining the SERS technique taught by Van Duyne (for measuring the Raman spectrum shift from a subdermal biosensor) and the SORS method, as taught by Mahadevan-Jansen and Morris (for measuring the shift in a spatially offset Raman spectrum),

was not thought to be practicable by persons of skill in the art prior to the filing of Appellants' application. As Dr. Van Duyne explains:

> Prior to the work described in the present application, it was believed that this increased angular distribution of the Raman signal in SERS would have been incompatible with the SORS technique. Mathematical models describing the combination of SERS and SORS were not available at that time (nor are they available today), so there was no way to predict their compatibility. Our grant application to help support the work described in the present application was actually turned down for this exact reason. Those deemed by a funding agency to be experts in the field did not believe that the scattering geometry produced by SERS would be compatible with SORS. Those in the field actually predicted that SERS and SORS could not be successfully combined and were therefore unwilling to provide support for such research.

Van Duyne Decl. ¶ 8. The inventive concept recited in Appellants' claims, therefore, is the combination of the SERS and SORS methods, which was thought impracticable at the time of invention, to measure the level of an analyte in an individual by determining the shift in the spatially offset Raman spectrum from a subdermally-implanted biosensor. We are not persuaded by the Examiner's finding that this is "well-understood, routine and conventional activity" or simple data collection, such as taking a blood sample or isolating a gene. To the contrary, Appellants claim a new technique hitherto considered unfeasible by persons of high skill in the art (i.e., funding agency grant reviewers, who are "deemed . . . to be experts in the field," Van Duyne Declaration ¶ 8).

We consequently conclude that Appellants' claims recite significantly more than merely the recitation of an abstract idea coupled with routine, well-understood data collection activity, but rather comprises an inventive concept that adds significantly more than just the abstract idea itself. We consequently reverse the Examiner's rejection on this ground.

B. Rejection of claims 1–20 under 35 U.S.C. § 103(a)

Appellants argue both rejections under Section 103(a) together, contending that the claims are not obvious over the combination of either Van Duyne and Mahadevan-Jansen or, alternatively Van Duyne and Morris. App. Br. 8. Appellants argue that, contrary to the Examiner's conclusion, a person of ordinary skill in the art would have had no reasonable expectation of success in combining the teachings of Van Duyne and Mahadevan-Jansen or Morris. *Id.* at 9.

Analysis

The Examiner finds that that Van Duyne teaches that the SERS technique is a process whereby the Raman scattering signal is increased when a Raman-active molecule is spatially confined within range of the electromagnetic fields generated upon excitation of the localized surface plasmon resonance of nanostructured noble metal surfaces. Ans. 13. The Examiner finds that SERS retains all of the advantages of normal Raman spectroscopy while achieving significantly stronger signal intensity. *Id.* (citing Van Duyne ¶ 49).

However, the Examiner finds, Van Duyne fails to explicitly disclose obtaining spatially offset measurements in order to obtain tissue depth sensitive information. Ans. 13. The Examiner finds that Mahadevan-Jansen teaches that the collection fiber is translationally movable along a straight line so that it is capable of collecting the Raman scattering light at various source-detector offsets. *Id.* at 13–14 (citing Mahadevan-Jansen Fig. 2). The Examiner concludes that it would have been obvious to a person of ordinary skill in the art to have modified the method and system of Van Duyne by utilizing spatially offset Raman spectroscopy (obtaining measurements at various source-detector offsets), with a reasonable

expectation of success, because an ordinary artisan would have recognized routine and conventional methods for obtaining spatially offset Raman spectra, as taught by Mahadevan-Jansen and suggested by Van Duyne. *Id.* at 14.

As an initial matter, Appellants argue that the Examiner has misunderstood the claim terms "Raman shift" and "spatially offset" and has incorrectly equated the terms. App. Br. 8. Appellants point to the Examiner's findings that: "Van Duyne et al. fails to disclose acquiring spatially offset Raman spectra," but that "light detected from a sample illuminated with a Raman spectrometer is necessarily 'Raman-shifted' (i.e., spatially offset)." *Id.* (quoting Final Act. 6, 7). According to Appellants, equating the Raman shift utilized in all forms of Raman spectroscopy with the spatial offset that is specific to spatially-offset Raman spectroscopy ("SORS") is a fundamental mischaracterization of these concepts. *Id.* at 8–9. Appellants point again to the Van Duyne Declaration, in which Dr. Van Duyne attests:

> The Office Action incorrectly equates the meanings of the terms of "Raman-shifted" and "spatially-offset." The Examiner appears to allege that because the Van Duyne et al. reference described the detection of Raman-shifted light, the reference necessarily describes the detection of spatially-offset light. This is not the case, and necessarily stems from a mischaracterization of one or both of these terms. Raman shift refers to a change in the energy in monochromatic light upon interaction with molecular vibrations, phonons or other excitations in a system. This energy shift provides information about the vibrational modes in the system. Spatially-offset Raman spectroscopy (SORS) refers to the collection of a Raman spectrum from a location that is spatially offset from the point of laser excitation. Acquiring a Raman spectrum does not necessarily entail collection of a spatially-offset Raman spectrum, unless specifically noted. Even though the light collected in the Van Duyne reference is "Raman-shifted" it was not "spatially offset." Any statement to the contrary is untrue.

Id. at 9 (quoting Van Duyne Decl. ¶ 5). Appellants contend that the Raman shift that is present in the methods described in Van Duyne et al. is not an inherent teaching or suggestion of spatial offset or SORS and that Van Duyne does not suggest spatial offset. *Id.*

Appellants argue further that there is nothing about the combination of SERS and SORS that would have been obvious or predictable, based on the understanding of an ordinary artisan at the time of the invention. App. Br. 10. In the Van Duyne Declaration, Dr. Van Duyne states that:

> As one who was working in the relevant fields at the time of the development of the presently claimed technology, I can attest to the fact that the successful combination of elements of these SERS and SORS into a single method for quantification of an analyte beneath the surface of a subject's skin was not predictable. In fact, I am not aware of any mathematical demonstration of the compatibility of these two techniques at the time of the invention, making it impossible to simulate experiments combining SERS and SORS, or to make educated predictions about the outcomes and/or success of such methods. In the absence of a mathematical description of the SERS and SORS together, predictions about the results of such a technique could not have been made; therefore, the success of the claimed methods was not predictable at the time of the present invention.

Id. (quoting Van Duyne Decl. ¶ 4). Appellants also point to Dr. Van Duyne's statement, quoted in Section A, *supra*, that, at the time of the filing of Appellants' application, persons of high skill in the art did not consider the combination of SERS and SORS practicable with any reasonable expectation of success. *Id.* (quoting Van Duyne Decl. ¶ 8 ("Those in the field actually predicted that SERS and SORS could not be successfully combined and were therefore unwilling to provide support for such research")).

Appellants assert that, contrary to the Examiner's findings, the changes in the means and manner of generating, reflecting, and collecting Raman signals have

complex consequences that are not easily predicted in the absence of mathematical descriptions of the techniques, which were not available at the time of the invention. App. Br. 11 (citing Van Duyne Decl. ¶¶ 4, 8). Consequently, Appellants argue, a person of ordinary skill in the art would have had no reasonable expectation of success in combining the teachings of Van Duyne and Mahadevan-Jansen, or Van Duyne and Morris, to arrive at Appellants' claimed invention. *Id.*

The Examiner responds that that it would have been obvious to a person of ordinary skill in the art at the time of the instant invention to have modified the method and system of Van Duyne by utilizing spatially offset Raman spectroscopy, with a reasonable expectation of success, because such an artisan would have recognized routine and conventional methods for obtaining spatially offset Raman spectra, as taught by Mahadevan-Jansen and suggested by Van Duyne. Ans. 12–13. Specifically, the Examiner concludes that a person of ordinary skill in the art would have reasonably expected this modification could have been made with predictable results, since both references teach the use of Raman spectral data and analysis, and that the rationale to combine the references would have been no more than the predictable use of prior art elements according to their established functions. *Id.* at 13 (citing *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007)).

We are not persuaded by the Examiner's reasoning. As an initial matter, in view of the Examiner's Answer to Appellants' arguments, we are not persuaded that the Examiner has erroneously confused and equated the claim terms "Raman shift" and "spatially offset," as Appellants argue. Nevertheless, we are not persuaded that the Examiner has met the burden of establishing a *prima facie* case of obviousness.

Van Duyne is directed to surface-enhanced Raman biosensors for detection of *in vivo* and *ex vivo* analytes and is silent with respect to spatially offset Raman spectroscopy ("SORS"), which Mahadevan-Jansen teaches: "comprises the steps of acquiring a plurality of spatially offset Raman spectra from the surgical site of interest, identifying tissue signatures from the plurality of spatially offset Raman spectra." Mahadevan-Jansen Abstr. Mahadevan-Jansen does not teach the use of either SERS or SORS for the detection of analytes, but rather teaches the use of SORS: "for surgical margin evaluation during breast conserving therapy and discriminating two layers of soft tissues." Mahadevan-Jansen ¶ 4. Although both Van Duyne and Mahadevan-Jansen are directed to using Raman spectroscopy as a diagnostic technique, the references employ different methodologies of measuring Raman spectrum shifts (i.e., surface-enhanced spectroscopy *versus* spatially-offset spectroscopy) for different purposes. More importantly, we are not persuaded by the Examiner's reasoning that a person of ordinary skill in the art would have been motivated to combine the teachings of the references with a reasonable expectation of success.

We find the Van Duyne Declaration to be important with respect to this issue in our analysis. Dr. Van Duyne attests, from personal experience, that: "the successful combination of elements of these SERS and SORS into a single method for quantification of an analyte beneath the surface of a subject's skin was not predictable." Van Duyne Decl. ¶ 4. Dr. Van Duyne further states that he was not aware: "of any mathematical demonstration of the compatibility of these two techniques at the time of the invention, making it impossible to simulate experiments combining SERS and SORS, or to make educated predictions about the outcomes and/or success of such methods." *Id.*

Dr. Van Duyne further states that he was not alone in believing that the SERS and SORS methodologies could not be combined with any reasonable expectation of success:

> Our grant application to help support the work described in the present application was actually turned down for this exact reason. Those deemed by a funding agency to be experts in the field did not believe that the scattering geometry produced by SERS would be compatible with SORS. Those in the field actually predicted that SERS and SORS could not be successfully combined and were therefore unwilling to provide support for such research.

Van Duyne Decl. ¶ 8. The reason for the skepticism was:

> The SERS technique produces a much broader angular signal distribution than conventional Raman spectroscopy techniques. This means that the reflected Raman signal is scattered over a much larger area when using SERS than when employing conventional Raman techniques. Prior to the work described in the present application, it was believed that this increased angular distribution of the Raman signal in SERS would have been incompatible with the SORS technique. Mathematical models describing the combination of SERS and SORS were not available at that time (nor are they available today), so there was no way to predict their compatibility.

Id. We find Dr. Van Duyne's testimony persuasive that, at the time of Appellants' filing of the instant application, it would not have been considered as practicable in the art to combine the SERS technique taught by Van Duyne and the SERS technique of Mahadevan-Jansen with a reasonable expectation of success.

Furthermore, Appellants' Specification discloses that:

> The solution provided by embodiments of the present invention removes the window and directly collect the SERS spectra transcutaneously. However, introducing the skin into the optical detection system presents a new set of challenges that have been overcome by the present invention. The large refractive index change between skin and air immediately produces light intensity losses due to

> back reflections. Within the skin layers, light is further attenuated due to multiple scattering and absorption events. These can be caused by lipids in cell walls, which scatter, blood, which absorbs, and proteins such as keratin and melanin which can both scatter and absorb light. These difficulties are further compounded when illuminating and collecting from a subcutaneous sample since both the input laser excitation light must pass through the skin and the output Raman scattered light must pass back out through the skin to reach the detector. The present invention addresses these issues with the use of spatially offset Raman spectroscopy (SORS).
>
> In SORS, Raman scattered light is collected from regions offset from the point of laser excitation at the sample. In contrast, for normal Raman spectroscopy the excitation and collection points are coincident so that the surface of the sample gives the greatest contribution to the Raman spectrum. When spectra are collected some distance away from the excitation point, spectral features originating from underlying layers give greater contribution than the surface. Combining the sensitivity of SERS with the depth resolution of SORS yields a powerful new tool for biomedical sensing.

Spec. 11–12 (internal references omitted). These disclosures of Appellants' Specification support Appellants' argument that the combination of SERS and SORS was a novel and innovative technique that was neither taught nor suggested by the cited prior art.

The Examiner has not effectively rebutted Appellants' arguments that the Examiner failed to establish a *prima facie* case of obviousness. We consequently reverse the Examiner's rejections of claims 1–20 upon this ground. Furthermore, Appellants and the Examiner rely upon the same arguments with respect to the Examiner's rejection of claims 1–20 on the ground of obviousness-type double patenting. The '226 patent, like Van Duyne, is directed to biosensors employing SERS methods. '226 patent Abstr. For the same reasons explained *supra*, we similarly reverse the Examiner's rejection of the claims upon that ground.

DECISION

The Examiner's rejection of claims 1–20 as unpatentable under 35 U.S.C. § 101 is reversed.

The Examiner's rejection of claims 1–20 as unpatentable under 35 U.S.C. § 103(a) is reversed.

The Examiner's rejection of claims 1–20 as unpatentable under the nonstatutory doctrine of obviousness-type double patenting is reversed.

REVERSED