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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte TOURADJ SOLOUKI

Appeal 2019-002402
Application 15/268,097
Technology Center 2800

Before ELIZABETH M. ROESEL, MICHAEL G. McMANUS, and MERRELL C. CASHION, JR., *Administrative Patent Judges*.

McMANUS, *Administrative Patent Judge*.

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] seeks review of the Examiner's decision to reject claims 1–13. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM IN PART.

[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as Baylor University. Appeal Br. 1.

CLAIMED SUBJECT MATTER

The present application generally relates to a system and method for mass spectrometry imaging. *See* Specification filed Sept. 16, 2016 ("Spec.") ¶ 6. Mass spectrometry ("MS") is taught to work "by ionizing compounds to generate charged molecules or molecule fragment ions and measuring their mass-to-charge ('m/z') ratios, which can be correlated to a particular atom, molecule, or compound." *Id.* ¶ 8. Appellant asserts that "[t]raditional MS removes ('desorbs')[2] elemental atoms or molecules from a surface of the material with high energy that at the same step ionizes the atoms or molecules to prepare them for the MS magnetic fields." Appeal Brief, filed Oct. 26, 2018 ("Appeal Br."), 1 (citing Spec. ¶ 9).

The Specification teaches a process of "applying different technologies by decoupling the desorption and ionization events." Spec. ¶ 18. The Specification further teaches that "first, a desorption technique, such as an ion beam, is applied to allow neutral molecules of the target sample to become desorbed from the surface without requiring the molecules to be ionized during the desorption." *Id.* The Specification additionally discloses that "[s]ubsequently, in the second stage and after the desorption and volatilization of defined targeted neutrals from the surface in the first stage, an ionization technique is applied so that the MS analysis can be focused on the ionized target molecules." *Id.*

[2] One of the cited references provides that "'desorption' refers to the departure of analyte from the surface and/or the entry of the analyte into a gaseous phase." Hutchens ¶ 135.

Claims 1 and 5 are illustrative of the subject matter on appeal and are reproduced below:

1. A system for mass spectrometry, comprising:

a desorption beam configured to desorb neutral molecules from a target of a material; and

an ionization source configured to ionize at least a portion of the neutral molecules after desorption from the target of the material to form ionized molecules, the ionization source being a radiofrequency ionization ("RFI") source.

5. A method of imaging a target molecule with a mass spectrometer, comprising:

desorbing one or more neutral molecules from a target of a material with a desorption beam configured to desorb neutral molecules; and

ionizing at least a portion of the neutral molecules into ionized molecules with a radiofrequency ionization ("RFI") source after the desorbing of the neutral molecules.

Appeal Br. 28–29 (Claims App.).

REFERENCES

The Examiner relies upon the following prior art:

Name	Reference	Date
Enke et al. ("Enke")	US 4,472,631	Sept. 18, 1984
Becker	US 4,920,264	Apr. 24, 1990
Hutchens et al. ("Hutchens")	US 2002/0037517 Al	Mar. 28, 2002
Franzen	US 2005/0017167 Al	Jan. 27, 2005
Chung et al. ("Chung")	US 2015/0235829 Al	Aug. 20, 2015

REJECTIONS

The Examiner maintains the following rejections:

1. Claims 1–7, 10, and 12 are rejected under 35 U.S.C. § 103 as being unpatentable over Becker in view of Chung. Final Action, dated May 30, 2018 ("Final Act."), 6–11.
2. Claim 8 is rejected under 35 U.S.C. § 103 as being unpatentable over Becker in view of Chung and further in view of Enke. *Id.* at 11–12.
3. Claim 9 is rejected under 35 U.S.C. § 103 as being unpatentable over Becker in view of Chung and further in view of Franzen. *Id.* at 12–13.
4. Claims 11 and 13 are rejected under 35 U.S.C. § 103 as being unpatentable over Hutchens in view of Chung. *Id.* at 13–17.

DISCUSSION

Rejection 1. The Examiner rejects claims 1–7, 10, and 12 as obvious over Becker in view of Chung. Final Act. 6–11. In support of the rejection, the Examiner finds that Becker teaches a system for mass spectrometry of a frozen solution target material by "exposing the frozen solution to a source

of desorbing energy such as a laser, an electron beam, an ion beam, or a source of fast atoms to desorb such large molecules from the surface of the frozen solution." *Id.* at 7 (citing Becker col. 4:44–48). The Examiner further finds that Becker teaches that the desorbed molecules may be neutral. Examiner's Answer, dated Nov. 27, 2018 ("Answer"), 5. The Examiner cites to the following portion of Becker as supporting the desorption of neutral molecules:

> If the energy source used to desorb the large molecules **does not also ionize the molecules**, the desorbed molecules may be exposed to a separate source of ionizing energy such as a photoionization source, e.g., a laser beam, to ionize the desorbed molecules prior to analyzing the molecules in a mass spectral analysis apparatus.

Becker col. 4:49–54 (emphasis added). The Examiner further finds that "although Becker generally discloses ionizing vaporized sample molecules . . . there is no explicit disclosure that the ionization source is a radiofrequency ionization ('RFI') source." Final Act. 7.

The Examiner relies on Chung as teaching "a method of radiofrequency ionization of ionizing vaporized molecules." *Id.* The Examiner cites to Chung's teaching that "the plasma of the plasma ionization device is a radiofrequency plasma (RF plasma) . . . As a result of a particularly gentle ionization via an RF plasma . . . it is likewise possible to ionize gas mixtures without fragmentation occurring." *Id.* (citing Chung ¶ 21).

The Examiner determines that a person of ordinary skill in the art would have had reason to modify the teachings of Becker so as to use the ionization step taught by Chung "in order to utilize a particular ionization

source capable of ionizing molecules without fragmenting the molecules for analyzing ionized molecules; the ionization mechanism of Chung having the advantage of ionizing without fragmenting, as is desired by Becker, which seeks to analyze ionized molecules." *Id.* at 8.

Appellant contends that the rejection is in error on several bases. First, Appellant argues that Becker does not teach "a desorption beam configured to desorb neutral molecules from a target of a material" because it teaches to use a high percentage of solvent and that the sample is "frozen to form a mixed matrix solution of the material sample and solvent." Appeal Br. 10. Appellant argues that, but for the frozen matrix, the beam of Becker would ionize the sample. *Id.*

In this regard, Appellant argues as follows:

> Only the <u>combination</u> of the high energy desorption beam and the frozen matrix solution together as a *system* allow Becker to reduce fragmentation of the sample. Thus, at best, it could be said that only the combination of a *system* is configured to minimize fragmentation of large molecules and avoid ionized molecules. In contrast, claim 1 and claim 5 require the <u>desorption</u> <u>beam</u> to be configured to desorb neutral molecules from a target of the material.

Id. (emphases in original). Appellant concludes that Becker fails to teach "a desorption beam configured to desorb neutral molecules" as required by independent claims 1 and 5. Appellant further argues that, as a result, Becker teaches away from claims 1 and 5. In determining whether Becker teaches such limitation, we consider the meaning of the term "a desorption beam configured to desorb neutral molecules."

The Specification teaches "a system and method for mass spectrometry imaging in a multi-stage ionization applying different technologies by decoupling the desorption and ionization events." Spec. ¶ 18. The Specification further teaches that the "system and method can act **independent of a matrix application** to the target sample for a direct analysis." *Id.* (emphasis added). That is, the Specification teaches that no matrix is required. Similarly, the Specification teaches that "[t]he system and method of the present invention may provide advantages over MALDI and SIMS of: . . . direct analysis **without the use of a matrix** applied to the sample that can contaminate the sample and cause intra-sample molecular migration to skew results." *Id.* (emphasis added).

The Specification discloses that "the desorption beam 18 can include an ion beam, cluster beam, or other source beam of sufficient resolution to dislodge accurately the intended target of the material 10 with molecules therefrom." Spec. ¶ 26. With regard to the power level of the beam the Specification teaches that "[t]he desorption beam 18 is sufficiently powered to desorb the molecules, but generally is used at a power level below the limit that the beam ionizes the molecules and thus can avoid fragmentation." *Id.*

Consistent with prior provisions, the Specification further teaches that "[b]ecause **the present system does not require a matrix substance to be overlaid onto the material** 10 as is currently done in MALDI techniques, the present system minimizes unwanted and potential reactions with solvent molecules, and analyte migrations associated with the use of ionization solvents or matrix reagents." Spec. ¶ 28 (emphasis added).

Certain dependent claims address desorption beams in the context of a matrix solution as follows:

> 11. The system of claim 1, wherein the desorption beam is configured to desorb neutral molecules from a target of a material **independent of a matrix solution** applied to the target.
>
> 13. The method of claim 5, wherein desorbing one or more neutral molecules from a target of a material comprises desorbing one or more neutral molecules from a target of a material **independently of a matrix solution** applied to the target.

Appeal Br. 29–30 (Claims App.). These dependent claims require that the desorbing step occur with respect to a target that does not include a matrix solution. A tribunal may consider the limitations of dependent claims in assessing the scope of the claims from which they depend. *See, e.g.*, *In re Tanaka*, 640 F.3d 1246, 1250 (Fed. Cir. 2011) ("Claims of narrower scope can be useful to clarify the meaning of broader, independent claims under the doctrine of claim differentiation.").

Considering all of the foregoing, and particularly the scope of dependent claims 11 and 13, we determine that the "desorption beam configured to desorb neutral molecules" of independent claims 1 and 5 is not limited to beams configured to desorb neutral molecules where the molecule is independent of a matrix solution. That is, we determine that the limitation may encompass both beams configured to desorb neutral molecules associated with a matrix solution and beams configured to be used without a matrix solution.

In view of such construction, we determine that Becker teaches a "desorption beam configured to desorb neutral molecules" and does not teach away from independent claim 1 or claim 5.

As its second argument, Appellant contends that the rejection is in error because the present invention requires that one "desorb generally intact molecules from a sample of material without fragmentation, and then ionize such molecules after the desorption" while Chung teaches only to ionize gas molecules. Appeal Br. 16.

In the Answer, the Examiner responds that the rejection relies upon Becker as teaching desorption and relies upon Chung "merely for teaching a radiofrequency ionization source." Answer 5. In its Reply Brief, Appellant does not directly contest the Examiner's findings but asserts that "the Examiner tries to apply Chung with Becker to the first element of claim 1 for a desorption beam." Reply Brief, filed Jan. 18, 2019 ("Reply Br."), 5. This is not an accurate characterization of the Examiner's rejection as clarified in the Answer. *See* Answer 5–6; *see also* Final Act. 7. Accordingly, Appellant's arguments in this regard are unpersuasive.

Third, Appellant additionally argues that there is insufficient reason to combine the teachings of Becker and Chung. Appeal Br. 16–17. Appellant argues that "Becker does not need Chung's low energy desorption beam, because Becker's high energy desorption beam is largely absorbed by the frozen matrix solution to minimize fragmentation." *Id.* at 16. Appellant further argues that "using Chung's low energy desorption beam, one with ordinary skill in the art would likely discard the frozen matrix solution in Becker." *Id.*

Appellant's arguments appear to be predicated on the notion that the Examiner relies upon Chung as teaching the first step of the method (desorbing). The rejection as stated in the Final Action indicates that the second step (ionization) is taught by Chung. *See* Final Act. 8 ("It would have been obvious to one possessing ordinary skill in the art at the time the invention was filed to have modified Becker using the ion source of Chung in order to utilize a particular ionization source capable of ionizing molecules without fragmenting the molecules for analyzing ionized molecules; the ionization mechanism of Chung having the advantage of ionizing without fragmenting, as is desired by Becker, which seeks to analyze ionized molecules."). Accordingly, Appellant has not shown error in this regard.

In view of the foregoing, we determine that Appellant has not shown error in the rejection of claims 1–7, 10, and 12 as obvious over Becker in view of Chung.

Rejections 2 and 3. Appellant includes headings in its brief regarding the rejections of claims 8 and 9 but does not present separate argument regarding such claims. Appeal Br. 17–18. Rather, Appellant relies upon the arguments it presents in regard to Rejection 1. As we have not found such arguments to be persuasive, we determine that Appellant has not shown error in the rejection of claims 8 and 9.

Rejection 4. The Examiner rejects claims 11 and 13 as obvious over Hutchens in view of Chung. Final Act. 13–17. Claims 11 and 13 depend from claims 1 and 5, respectively, and each additionally requires desorbing

neutral molecules "from a target of a material independent[ly] of a matrix solution applied to the target." Appeal Br. 29–30 (Claims App.).

The Examiner finds that Hutchens teaches "a desorption beam configured to desorb neutral molecules from a target of a material . . . and an ionization source configured to ionize at least a portion of the neutral molecules after desorption." Final Act. 13. The Examiner further finds that Hutchens lacks an "explicit disclosure that the ionization source is a radiofrequency ionization ('RFI') source." *Id.* at 14. The Examiner additionally finds that Chung discloses a method of radiofrequency ionization of vaporized molecules. *Id.*

The Examiner determines that one of ordinary skill in the art would have had reason to modify the teachings of Hutchens "in order to utilize a particular ionization source capable of ionizing molecules without fragmenting the molecules for analyzing ionized molecules; the ionization mechanism of Chung having the advantage of ionizing without fragmenting, as is desired by Hutchens, which seeks to analyze ionized molecules." *Id.* at 14. In the Answer, the Examiner finds that "one of ordinary skill in the art would have recognized that the ionization mechanism of Chung would be an obvious mechanism for embodying the ionizer of Hutchens, with the added benefit that the radiofrequency ionization of Chung provides soft ionization without fragmenting a sample." Answer 9.

Appellant argues that the rejection is in error on several bases. Appeal Br. 18–27. First, Appellant argues that "*Hutchens consistently describes the desorption/ionization process of the analyte in a single event with one or more lasers.*" *Id.* at 22 (emphasis in original); *see also id.* at 22–25. The Examiner acknowledges that "Hutchens is primarily concerned"

with an embodiment where a laser both desorbs and ionizes the analyte in a single step. Answer 7. The Examiner, however, finds that Hutchens additionally "discloses separating the desorption and ionization processes so as to perform desorption from the solid phase into a gas/vapor phase." *Id.* In support, the Examiner cites to the following portion of Hutchens:

> Further, a sample presenting means (composed of one or more of the suitable probe element materials described in previous claims), wherein analyte(s) are bound to the surface said sample presenting means by one or more photolabile bonds so that incident pulse(s) of light (e.g., from one or more lasers) is used to break the photolabile bond(s) tethering the analyte(s) to the probe element surface in a manner that is consistent with the subsequent desorption of the analyte from the stationary (solid) phase surface of the probe into the gas (vapor) phase is also presented.

Answer 8 (quoting Hutchens ¶ 122).

The Examiner additionally cites to Hutchens' teaching of "a laser beam, to vaporize the analyte from the surface of a probe tip. In the process, some of the molecules are ionized," (Hutchens ¶ 164) and infers that, therefore, at least some of the molecules are desorbed without being ionized. Answer 8. The Examiner further cites Hutchens' teaching that "[o]ne skilled in the art recognizes that other modes of detection and ionization can also be used." *Id.* (citing Hutchens ¶ 164).

We find the Examiner's reasoning unpersuasive. Each of the cited teachings, considered in context, indicates that Hutchens contemplates a single entity—a laser beam—for performing both desorption and ionization. It is true that Hutchens suggests that ionization may be incomplete (Hutchens ¶ 164) but this does not represent a teaching in Hutchens of a

separate ionization step, nor an ionization source that is separate from the desorption beam.

Appellant further argues that, in view of Hutchens' teaching of desorption and ionization in a single step with a single laser beam, there is insufficient reason that one of skill in the art would have combined the teachings of Hutchens and Chung. Appeal Br. 26. Appellant argues that "Hutchens both desorbs and ionizes with the same laser applied to the surface having the analyte." *Id.* Appellant further argues that "Chung's ionization with a low energy is not needed for Hutchens—the Hutchens' analyte is already ionized." *Id.*

We find this reasoning persuasive. The Examiner does not provide adequate reasoning why one skilled in the art would have added the ionization step of Chung to the process of Hutchens. The Examiner finds that the ionization step of Chung "would be an obvious mechanism for embodying the ionizer of Hutchens." Answer 9. If this is construed to mean that the radiofrequency ionization of Chung is substituted for the laser of Hutchens, then the process lacks a desorption step. If, instead, the Examiner finds that one of skill in the art would have applied the ionization step of Chung subsequent to the laser desorption and ionization step of Hutchens, then the Examiner fails to explain the benefit of a second ionization step. That is, the Examiner does not explain how or why one of skill in the art would implement a system with two ionization steps nor does the Examiner cite to any prior art with such a two-step ionization process.

The present rejection differs from those rejections predicated upon the combination of the teachings of Becker and Chung because Becker teaches a desorption step followed by an ionization step. *See* Becker 4:9–18. The

combination of Becker and Chung requires only the substitution of the ionization step of Chung for the ionization step of Becker. In contrast, the present rejection appears to require laser ionization followed by radiofrequency ionization without adequate explanation of the need for a second ionization step.

Accordingly, we determine that the Examiner has not adequately shown that one of skill in the art would have had reason to combine the teachings of Hutchens and Chung.

Additionally, Appellant argues that the combination of Hutchens and Chung does not teach "a desorption beam configured to desorb neutral molecules." Appeal Br. 26–27. Appellant argues that the proposed combination would yield a system configured to desorb ions, not neutral molecules. *Id.*

The term "configured to" indicates that a claim element is designed or constructed for a certain purpose. *See Aspex Eyewear, Inc. v. Marchon Eyewear, Inc.*, 672 F.3d 1335, 1349 (Fed. Cir. 2012); *see also Acclarent, Inc. v. Albritton*, No. IPR2017-00498, 2018 WL 3374755, at *6 (P.T.A.B. July 9, 2018) ("We agree with Patent Owner that the most natural reading of 'configured to' in the claims at issue here requires structure designed to accomplish the claimed objectives."). Hutchens teaches that "there is provided in accordance with the present invention . . . laser beam means for producing a laser beam directed to said analyte sample ***for imparting sufficient energy to desorb and ionize a portion of said analyte molecules*** from said analyte sample." Hutchens ¶ 24 (emphasis added). Hutchens later teaches that during the vaporization process "some of the molecules are ionized." *Id.* ¶ 64. The Examiner relies on this teaching that "some" (rather

than all) molecules are ionized to find that Hutchens teaches a beam "configured to desorb neutral molecules." The Examiner's finding is not persuasive. The Examiner has not cited to sufficient evidence that Hutchens teaches a beam designed or constructed to desorb neutral molecules. Further, the explicit teaching of Hutchens is to provide a laser beam "imparting sufficient energy to desorb and ionize a portion of said analyte molecules." *Id.* ¶ 24.

In view of the foregoing, we determine that the Examiner has not shown an adequate reason why one of skill in the art would have combined the teachings of Hutchens and Chung nor has the Examiner shown that such combination would yield "a desorption beam configured to desorb neutral molecules" as required by independent claims 1 and 5 and, therefore, dependent claims 11 and 13.

CONCLUSION

The Examiner's rejections of claims 1–10, and 12 are affirmed. The Examiner's rejection of claims 11 and 13 is reversed.

In summary:

Claims Rejected	**35 U.S.C. §**	**Reference(s)/Basis**	**Affirmed**	**Reversed**
1–7, 10, 12	103	Becker, Chung	1–7, 10, 12	
8	103	Becker, Chung, Enke	8	
9	103	Becker, Chung, Franzen	9	
11, 13	103	Hutchens, Chung		11, 13
Overall Outcome			1–10, 12	11, 13

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 IN PART