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DINSMORE & SHOHL LLP
755 WEST BIG BEAVER RD
SUITE 1900
TROY, MI 48084

EXAMINER
KUMAR, PREETI

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jennifer.baker@dinsmore.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte PING WANG, MINJUAN ZHANG, HONGFEI JIA, ARCHANA H. TRIVEDI, and MASAHIKO ISHII

Appeal 2023-003255
Application 16/258,556
Technology Center 1700

Before CATHERINE Q. TIMM, CHRISTOPHER C. KENNEDY, and JEFFREY R. SNAY, *Administrative Patent Judges.*

TIMM, *Administrative Patent Judge.*

DECISION ON APPEAL

STATEMENT OF THE CASE

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from the Examiner's decision to reject claims 1–13. *See* Final Act. 1. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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[1] "Appellant" refers to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real parties in interest as Toyota Motor Corporation and The University of Akron. Appeal Br. 2.

CLAIMED SUBJECT MATTER

The claims are directed to a process including a step of binding a protein to the surface of a solid substrate by a linker moiety. Claim 1, reproduced below, illustrates the claimed subject matter:

> 1. A process for stabilizing a protein against thermal inactivation, comprising:
>
> binding a protein to the surface of a solid substrate;
>
> the protein bound to the surface by a linker moiety between an active group of the protein and said substrate, wherein the linker comprises a bond formed from [one] or more active groups selected from the group consisting of alcohol, thiol, carboxylic acid, anhydride, epoxy, and ester, and wherein said bond of the protein to the solid substrate stabilizes the protein against thermal inactivation.

Appeal Br. 14 (Claims App.).

REFERENCES

The Examiner relies on the following references to reject the claims:

Name	Reference	Date
Dordick	US 6,291,582 B1	Sept. 18, 2001
Powers	US 6,342,386 B1	Jan. 29, 2002
Wu	US 10,767,141 B2	Sept. 8, 2020
Wang	US 10,781,438 B2	Sept. 22, 2020
Ermantraut	US 2003/0161789 A1	Aug. 28, 2003
Ikawa	US 2004/0053354 A1	Mar. 18, 2004
Hall	Hall, D.B., Underhill, P. and Torkelson, J.M. (1998), *Spin coating of thin and ultrathin polymer films*, Polym. Eng. Sci., 38: 2039–2045. https://doi.org/10.1002/pen.10373	Apr. 8, 2004
Minier	Miner et al., *Covalent Immobilization of Lysozyme on Stainless Steel. Interface Spectroscopic Characterization and*	May 18, 2005

	Measurement of Enzymatic Activity, *Langmuir* 2005, 21, 13, 5957–5965 https://doi.org/10.1021/la0501278	

REJECTIONS

The Examiner maintains the following rejections:[2]

A. Claims 1–9 and 13 under pre–AIA 35 U.S.C. § 103(a) as obvious over Ikawa (Final Act. 10; Ans. 3);

B. Claims 1–7 and 13 under pre–AIA 35 U.S.C. § 103(a) as obvious over Minier (Final Act. 11; Ans 5);

C. Claims 8 and 10–12 under pre–AIA 35 U.S.C. § 103(a) as obvious over Minier and Ermantraut (Final Act. 15; Ans. 8);

D. Claims 8 and 9 under pre–AIA 35 U.S.C. § 103(a) as obvious over Minier and Hall (Final Act. 16; Ans. 9);

E. Claims 1–13 on the ground of nonstatutory double patenting as unpatentable over claims 1–9 and 14 of Wu (Final Act. 18; Ans. 10); and

F. Claims 1–13 on the ground of nonstatutory double patenting as unpatentable over claims 8–13 of Wang (Final Act. 18; Ans. 10).

[2] The Examiner withdrew a number of rejections after the Final Office Action. *See* Pre-Brief Appeal Conference Decision of Nov. 17, 2022 at p. 2; Ans. 11.

OPINION

Rejection A: Obviousness over Ikawa

Turning first to the rejection of claims 1–9 and 13 as obvious over Ikawa, we frame the issue as: Has Appellant identified a reversible error in the Examiner's finding that Ikawa teaches a linker moiety comprising one or more of the active groups recited in claim 1?

Appellant has identified such an error.

The claims require binding a protein to the surface of a solid substrate by a linker moiety that comprises "a bond formed from [one] or more active groups selected from the group consisting of alcohol, thiol, carboxylic acid, anhydride, epoxy, and ester." *See* claim 1.

In rejecting claims 1–9 and 13 as obvious over Ikawa (Final Act. 10; Ans. 3), the Examiner finds that Ikawa teaches the required binding, citing paragraphs 53–61 for a teaching of binding a protein to a surface by a linker moiety and paragraph 127 as teaching claim 1's active groups. Final Act. 10; Ans. 3.

We agree with Appellant that paragraph 127 does not support the Examiner's finding. Appeal Br. 7. The Examiner is attempting to combine unrelated teachings within Ikawa. Although Ikawa's paragraph 53 provides evidence that it was known in the art to form covalent bonds between ligands (proteins) and carrier substrates, paragraph 53 does not detail how this bonding was accomplished. The Examiner turns to paragraph 127, but this paragraph does not relate to the covalent bonding process disclosed in paragraph 53. In fact, paragraph 127 is not concerned with bonding between a protein and substrate at all. Instead, paragraph 127 describes preferred

polymer materials containing a photoreactive component Ikawa uses in a material of optical immobilization. Ikawa ¶ 127. This photopolymer immobilizes very small objects by photoinduced deformation during light irradiation. Ikawa ¶ 118. Thus, the photopolymer is part of the substrate. The groups and formulas discussed in paragraph 127 are within the polymer substrate and not active groups forming a bond between the protein and the substrate.

Not only is paragraph 127's bonding not between a protein and a substrate, Ikawa seeks to use a different material of optical immobilization when the very small object is a biological substance. Ikawa ¶ 121 ("In case that very small object to be immobilized is a biological substance, of which the activity may be deteriorated via the chemical reaction with the carrier material, photoisomerization-potential components are preferable as the photoreactive components."). That is, paragraph 127 discloses a substrate material different than the one used in a substrate that immobilizes proteins. Paragraph 127 does not support the Examiner's finding that Ikawa teaches an active group from the genus of the claims as a linker moiety between a protein active group and the substrate as required by the claims.

Because the Examiner has not provided evidence that Ikawa would have taught or suggested bonding a protein to a substrate with one of claim 1's active group linker moieties, we agree with Appellant that a preponderance of the evidence on this appeal record fails to support the Examiner's rejection over Ikawa.

Rejection B: Obviousness over Minier

Turning next to the Examiner's rejection of claims 1–7 and 13 as obvious over Minier (Final Act. 11; Ans. 5), we determine two issues arise:

1) Has Appellant identified a reversible error in the Examiner's finding that Minier's process of binding a HEWL protein to the surface of a stainless-steel substrate meets the requirement of stabilizing the protein against thermal inactivation (Final Act. 12); and
2) Has Appellant identified a reversible error in the Examiner's finding that Minier's alcohol active group bound to the substrate as shown in Figure 1 is an active group within the meaning of claim 1 (Ans. 13)?

Both issues resolve based on a proper interpretation of claim 1. "[T]he PTO must give claims their broadest reasonable construction consistent with the specification." *In re ICON Health & Fitness, Inc*., 496 F.3d 1374, 1379 (Fed. Cir. 2007). "[A]s applicants may amend claims to narrow their scope, a broad construction during prosecution creates no unfairness to the applicant or patentee." *Id.*; *see also In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989) ("[D]uring patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.").

Issue 1: Thermal Stability

Appellant contends that "[n]owhere does Minier teach or suggest the claimed stabilization of the protein against thermal inactivation as is presented in claim 1." Appeal Br. 10. We agree, but it is of no moment

because thermal stability is not an additional limitation on the process of the claim.

Although claim 1 introduces the process as a process for stabilizing a protein against thermal inactivation, the body of the claim recites a single process step, which is a step of binding a protein to the surface of a solid substrate by a linker moiety that comprises "a bond formed from [one] or more active groups selected from the group consisting of alcohol, thiol, carboxylic acid, anhydride, epoxy, and ester." Appeal Br. 14 (Claims App.). The body of the claim then recites the function of the bond, i.e., it "stabilizes the protein against thermal inactivation." *Id.*

The Specification provides evidence that the bond itself provides the recited thermal stability. Spec. ¶ 48 ("It appeared that covalent cross-linked enzyme afforded better stability against thermal inactivation, as compared to physical adsorbed enzyme."). Thus, we determine that the thermal stability limitation, in fact, does not impose an additional requirement on the claimed invention, i.e., does not narrow the claim, but is a property necessarily present due to covalent bonding. A reference teaching bonding between the protein and substrate will meet the thermal stability requirement. *See In re Kubin*, 561 F.3d 1351, 1357 (Fed.Cir.2009); *Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1369 (Fed. Cir. 2012).

Minier teaches that it was known in the art to covalently bond proteins onto substrates through alcohol groups on the substrate, grafting of reactive amino groups, and crosslinking of the proteins using dialdehyde glutaraldehyde (GA). Minier 5958 col. 1 ¶ 2; Fig. 1. The covalent bonds would have inherently stabilized the protein against thermal inactivation as required by claim 1.

Appellant has not identified a reversible error in the Examiner's finding that Minier's process of binding a HEWL protein to the surface of a stainless-steel substrate meets the requirement of stabilizing the protein against thermal inactivation (Final Act. 12).

Issue 2: Active Group

Next, we turn to the question of whether Appellant has identified a reversible error in the Examiner's finding that the Minier's alcohol active group bound to the substrate as shown in Figure 1 is an active group within the meaning of claim 1.

We determine that claim 1 encompasses Minier's alcohol active group and, thus, Appellant has not identified a reversible error.

Claim 1's process has one step, a step of binding a protein to the surface of a solid substrate. Binding is by a linker moiety. Claim 1 further limits the location of the linker moiety and its structure. The location is "between an active group of the protein and said substrate." Appeal Br. 14 (Claims App.). The linker moiety structure "comprises a bond formed from [one] or more active groups selected from the group consisting of alcohol, thiol, carboxylic acid, anhydride, epoxy, and ester." *Id.*

The Meaning of "Active Group"

Interpreting "active groups" consistently with the Specification, we determine that active groups are groups that form covalent bonds with other active groups. The Specification describes active groups on polymers and substrates as forming covalent bonds with the protein's active groups, i.e., free amines. Spec. ¶¶ 16, 29, 33.

The Location of the Active Group

Claim 1 limits the location of the linker moiety to "between *an active group of the protein* and *said substrate*." Claim 1 (emphasis added). The word "between" allows the location to be anywhere between the protein's active group and the substrate.

The next clause of the claim — "wherein the linker comprises a bond formed from [one] or more active groups selected from the group consisting of alcohol, thiol, carboxylic acid, anhydride, epoxy, and ester" — requires a bond formed from an active group, i.e., a group that forms a covalent bond with another active group. Appeal Br. 14 (Claims App.). But this clause does not further limit the active group with which it reacts.

We reiterate that claim 1 merely recites that the linker moiety is *between* the protein's active group and *the substrate*. Claim 1 does not recite that the linker moiety is between the active group of the protein and *the active groups selected from the group consisting of* alcohol, thiol, carboxylic acid, anhydride, epoxy, and ester.

Appellant contends that Minier teaches an aldehyde linking group, a group not recited in claim 1. Appeal Br. 12. That is true, but given the above claim interpretation, we agree with the Examiner that Minier's Figure 1 depicts a substrate with an alcohol as an active group that reacts with silane triol (APS) that condenses to form polysiloxane, which in turn is crosslinked with the protein using dialdehyde glutaraldehyde (GA). Appellant is correct that there is an aldehyde active group that directly reacts with the HEWL protein, but the problem is that claim 1 sweeps-in the alcohol active group. This is because claim 1 does not clearly require a direct linkage to the

HEWL protein between the free-amine active group and the linker active group. Claim 1 only requires an active group somewhere (anywhere) between the protein and *the substrate*.

Thus, Appellant has not identified a reversible error in the Examiner's finding that Minier teaches claim 1's linker.

Rejection C: Obviousness over Minier and Ermantraut

We now turn to the rejection of claims 8 and 10–12 over Minier and Ermantraut. Final Act. 15; Ans. 8.

Claims 8 and 10–12 require binding be performed by spin coating the protein onto the surface (claim 8) or binding comprising spin coating a first solution comprising the protein onto the surface (claim 10).

The Examiner acknowledges that Minier does not teach the required spin coating and turns to paragraph 16 of Ermantraut to support a finding that "spincoating with glutaraldehyde and protease is a commonly known process of application of a thin biopolymeric layer to a substrate in general." Final Act. 15.

We agree with Appellant that Ermantraut's paragraph 16 does not teach spin coating protease. Appeal Br. 12. As Appellant points out, paragraph 16 teaches forming a biopolymeric layer by spin coating gelatin in water containing 5% glutaric dialdehyde. Ermantraut ¶ 16. Although protease is present later, it is not in any spun coated solution, it is a component of a bath into which the biopolymeric layer is immersed (after further coating with an image photoresist). As Appellant states, nowhere in Ermantraut's paragraph 16 is a protease spin coated onto a surface.

Appellant has identified a reversible error in the Examiner's rejection of claims 8 and 10–12 as obvious over Minier and Ermantraut.

Rejection D: Obviousness over Minier and Hall

We now turn to the Examiner's rejection of claims 8 and 9 over Minier and Hall (Final Act. 16; Ans. 9).

As we state above, claim 8 requires binding be performed by spin coating the protein onto the surface. The Examiner finds that Hall teaches spin coating ultrathin polystyrene on silicon substrates. Final Act. 16, citing Hall 2040 col. 1, last para. Appellant contends that Hall's teaching "is nothing more than a simple recognition that spin coating was commonly known" and Minier and Hall fail to teach spin coating a protein on a surface. Appeal Br. 12.

We agree with Appellant that the Examiner has not established the obviousness of spin coating protein in the context of Minier's process. Hall merely teaches spin coating polystyrene films from toluene onto silicon substrates. Hall 2040 col. 1, last para. Minier uses a dipping method. Minier 5959 col. 1 (Immobilization of HEWL). The Examiner has not provided a reasonable rationale supporting the obviousness of spin coating Minier's HEWL protein. Appellant has identified a reversible error in the Examiner's rejection of claim 8 over Minier and Hall.

Claim 9 does not depend from claim 8, but instead depends from claim 1. Claim 9 requires the surface comprise polystyrene. Appellant does not argue against the rejection of claim 9. Thus, Appellant has not identified a reversible error in the rejection of claim 9 over Minier and Hall.

Nonstatutory Double Patenting

The Examiner rejects claims 1–13 on the ground of nonstatutory double patenting as being unpatentable over claims 1–9 and 14 of Wu (US 10,767,141 B2) and over claims 8–13 of Wang (US 10,781,438 B2). Final Act. 18; Ans. 10.

Wu

In rejecting claims 1–13 over Wu, the Examiner determines that the claims "are not patentably distinct from each other because the liquid coating material of the patented claims has the same protein encompassed in the method of the instant claims bound to the surface." *Id.*

The Examiner has failed perform the required non-statutory double-patenting analysis.

The key question in any obviousness double patenting analysis is: "Does any claim in the application define merely an obvious variation of an invention claimed in the patent asserted as supporting double patenting?" *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1278 (Fed. Cir. 1992) (discussing *In re Vogel*, 422 F.2d 438 (CCPA 1970)). Answering this question requires that the decisionmaker first construe the claims in the patent and the claims under review and determine the differences between them. *Eli Lilly & Co. v. Barr Labs*., *Inc*., 251 F.3d 955, 970 (Fed. Cir. 2001). After determining the differences, the decisionmaker must determine whether the differences in subject matter render the claims patentably distinct. *Id*. Where the subject matter of a pending claim under review is an obvious variation of the subject matter of a patented claim, the pending claim is not patentably distinct. *In re Vogel*, 422 F.2d 438, 441

(CCPA 1970). But "there must be some clear evidence to establish why the variation would have been obvious which can properly qualify as 'prior art'." *In re Kaplan*, 789 F.2d 1574, 1580 (Fed. Cir. 1986).

The Examiner points out the similarities between Appellant's claims and those of Wu, but does not provide evidence that the differences would have been obvious. And the differences are substantial. Wu's claims 1–9 and 14 recite a method of facilitating the removal of a biological stain on a substrate or coating comprising providing a liquid coating material containing alcohol associated with thermolysin-like protease to form a liquid bioactive coating material. Appellant's claims recite a process for stabilizing a protein against thermal inactivation involving binding a protein to the surface of a solid substrate. A method of providing a liquid coating material for removing stains is quite different from a process involving binding a protein to a substrate. The Examiner does not perform the required obviousness analysis accounting for those differences.

Wang

The non-statutory double-patenting rejection of claims 1–13 over Wang is summarily sustained given that Appellant intends to perfect the terminal disclaimer filed July 5, 2023 disapproved on July 6, 2023. Hr'g Tr. 13:4–6 ("And then as to the '438 reference, the '438 Patent, we filed a terminal disclaimer. We recognize that it was disapproved, but we will go ahead and we will address that this week.").

CONCLUSION

The Examiner's decision to reject claims 1–13 is AFFIRMED.

DECISION SUMMARY

The following table summarizes our decision:

Claim(s) Rejected	35 U.S.C. §	Reference(s)/ Basis	Affirmed	Reversed
1–9, 13	103	Ikawa		1–9, 13
1–7, 13	103	Minier	1–7, 13	
8, 10–12	103	Minier, Ermantraut		8, 10–12
8, 9	103	Minier, Hall	9	8
1–13		Nonstatutory Double Patenting, Wu		1–13
1–13		Nonstatutory Double Patenting, Wang	1–13	
Overall Outcome			1–13	

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a)(1)(iv) (2022).

AFFIRMED