

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,
Petitioner,

v.

THE CHINESE UNIVERSITY OF HONG KONG,
Patent Owner.

IPR2024-00028
Patent 11,091,794 B2

Before DEBORAH KATZ, MICHAEL J. FITZPATRICK, and
JAMIE T. WISZ, *Administrative Patent Judges*.

FITZPATRICK, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Petitioner, Pacific Biosciences of California, Inc., filed a Petition to institute an *inter partes* review of claims 1–19 of U.S. Patent No. 11,091,794 B2 (“the ’794 patent”) pursuant to 35 U.S.C. § 311(a). Paper 2 (“Pet.”). Patent Owner, The Chinese University of Hong Kong, filed a Preliminary Response pursuant to 37 C.F.R. § 42.107(b). Paper 6 (“Prelim. Resp.”).

Institution of an *inter partes* review requires “a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). Determining whether a reasonable likelihood has been met has been delegated to the Board. *See* 37 C.F.R. § 42.4(a) (“The Board institutes the trial on behalf of the Director.”). For the reasons explained below, there is a reasonable likelihood that Petitioner would prevail with respect to at least one claim. Accordingly, we grant the Petition.

A. Related Matters

The parties identify the following district court proceeding involving the ’794 patent, *Take2 Technologies Limited et al. v. Pacific Biosciences of California, Inc.*, No. 5:23-cv-041661 (N.D. Cal.) (the “related lawsuit”). Pet. 74; Paper 5, 2.

B. Real Parties In Interest

Petitioner identifies itself as the sole real party in interest. Pet. 74.

Patent Owner identifies The Chinese University of Hong Kong and Take2 Technologies Limited as the real parties in interest. Paper 5, 1. Patent Owner states that “The Chinese University of Hong Kong is a university established by legislation in the Hong Kong Special

Administrative Region (‘Hong Kong SAR’) located in Shatin, New Territories, Hong Kong SAR.” *Id.* Patent Owner states that “Take2 Technologies Limited is a wholly owned subsidiary of Take2 Holdings Limited” of Grand Cayman, Cayman Islands. *Id.*

C. The ’794 Patent

The ’794 patent is titled “Determination of Base Modifications of Nucleic Acids.” Ex. 1001, code (54). “The most common base modifications are the addition of a methyl group to different DNA bases at different positions, so-called methylation.” *Id.* at 1:39–41. Methylation “has notable roles in gene expression and silencing, embryonic development, transcription, chromatin structure, X chromosome inactivation, protection against activity of the repetitive elements, maintenance of genomic stability during mitosis, and the regulation of parent-of-origin genomic imprinting.” *Id.* at 1:53–58. Thus, it was known that “accurate measurement of methylomic modification on DNA molecules would have numerous clinical implications.” *Id.* at 2:3–5. Two techniques had been developed in the prior art for measuring or detecting whether and which bases in DNA molecules were methylated. *Id.* at 2:5–18. However, both techniques were “bisulfite-based,” which carried certain disadvantages. *Id.* at 2:19–31.

The ’794 patent describes and claims “a new method that, in one embodiment, allows the determination of base modifications, such as 5mC [i.e., 5-methylcytosine] in nucleic acids” without the disadvantages described in the prior art. *Id.* at 2:35–39; *see also* Prelim. Resp. 4 (“The ’794 patent discloses, *inter alia*, methods for determining nucleotide modifications, e.g., methylation of DNA nucleotides.”). The ’794 patent

states that its invention “can be used for . . . single molecule, real-time [‘SMRT’] sequencing in which the progress of the sequencing of a single DNA molecule is monitored in real-time.” *Id.* at 2:54–58.

It cannot be reasonably disputed, nor does Patent Owner dispute, that SMRT sequencing was known in the art before the claimed invention of the ’794 patent. For example, in 2010, one prior art reference (Flusberg) summarized SMRT sequencing and how it works as follows:

We describe the direct detection of DNA methylation, without bisulfite conversion, through single-molecule, real-time (SMRT) sequencing. In SMRT sequencing, DNA polymerases catalyze the incorporation of fluorescently labeled nucleotides into complementary nucleic acid strands. The arrival times and durations of the resulting fluorescence pulses yield information about polymerase kinetics and allow direct detection of modified nucleotides in the DNA template, including N6-methyladenine, 5-methylcytosine and 5-hydroxymethylcytosine. Measurement of polymerase kinetics is an intrinsic part of SMRT sequencing and does not adversely affect determination of primary DNA sequence. The various modifications affect polymerase kinetics differently, allowing discrimination between them. We used these kinetic signatures to identify adenine methylation in genomic samples and found that, in combination with circular consensus sequencing, they can enable single-molecule identification of epigenetic modifications with base-pair resolution. This method is amenable to long read lengths and will likely enable mapping of methylation patterns in even highly repetitive genomic regions.

Ex. 1006, Abstract.

According to Patent Owner, “Claim 1 of the ’794 patent relates to the discovery of a method employing a unique combination of some of the data from SMRT sequencing that could be used to detect base modifications, and in particular detect methylated cytosine, to a much higher degree of accuracy than prior art methods.” Prelim. Resp. 4. The purportedly unique

combination of data is recited in claim 1 in the form of “an input data structure” that “includes a window of nucleotides around a target nucleotide (the putative modified base) and for each nucleotide in that window the identity of the nucleotide (A, C, G or T^[1]), the position of the nucleotide relative to the target, the width of the pulse associated with the nucleotide (PW), and the interpulse duration (IPD).” *Id.* at 4–5.

D. The Challenged Claims

Inter partes review is sought for claims 1–19, which is all of the claims of the ’794 patent. Pet. 1. Claim 1 is the sole independent claim and is reproduced below.

1. A method for detecting a modification of a nucleotide in a nucleic acid molecule, the method comprising:

(a) receiving data acquired by measuring pulses in an optical signal corresponding to nucleotides sequenced in a sample nucleic acid molecule and obtaining, from the data, values for the following properties:

for each nucleotide:

an identity of the nucleotide,

a position of the nucleotide within the sample nucleic acid molecule,

a width of the pulse corresponding to the nucleotide, and

an interpulse duration representing a time between the pulse corresponding to the nucleotide and a pulse corresponding to a neighboring nucleotide;

(b) creating an input data structure, the input data structure comprising a window of the nucleotides sequenced in the sample nucleic acid molecule, wherein the input data

¹ These letters respectively refer to the following nucleotides (or bases): adenine, cytosine, guanine, and thymine. See Ex. 1001, 1:42.

structure includes, for each nucleotide within the window, the properties:

the identity of the nucleotide,

a position of the nucleotide with respect to a target position within the window,

the width of the pulse corresponding to the nucleotide, and

the interpulse duration;

(c) inputting the input data structure into a model, the model trained by:

receiving a first plurality of first data structures, each first data structure of the first plurality of data structures corresponding to a respective window of nucleotides sequenced in a respective nucleic acid molecule of a plurality of first nucleic acid molecules, wherein each of the first nucleic acid molecules is sequenced by measuring pulses in the optical signal corresponding to the nucleotides, wherein the modification has a known first state in a nucleotide at a target position in each window of each first nucleic acid molecule, each first data structure comprising values for the same properties as the input data structure,

storing a plurality of first training samples, each including one of the first plurality of first data structures and a first label indicating the first state of the nucleotide at the target position, and

optimizing, using the plurality of first training samples, parameters of the model based on outputs of the model matching or not matching corresponding labels of the first labels when the first plurality of first data structures is input to the model, wherein an output of the model specifies whether the nucleotide at the target position in the respective window has the modification,

(d) determining, using the model, whether the modification is present in a nucleotide at the target position within the window in the input data structure.

Ex. 1001, 115:38–116:61.

E. Asserted Patents and Printed Publications

Name	Reference	Ex. #
Flusberg	<i>Direct Detection of DNA Methylation During Single-molecule, Real-Time Sequencing</i> , NATURE METHODS 7(6) (June 2010) ²	1006
Flusberg '338	US 9,175,338 B2, issued Nov. 3, 2015	1007
PacBio-BAM	BAM Format Specification for PacBio, PacBioFileFormats 5.0 Documentation, http://web.archive.org/web/20170916112547/http://pacbiofileformats.readthedocs.io/en/5.0/BAM.html (archived Sept. 16, 2017)	1011
Clement	US 2016/0326593 A1, published Nov. 10, 2016	1018
Template Guide	Pacific Biosciences Template Preparation and Sequencing Guide, https://www.pacb.com/wp-content/uploads/2015/09/Guide-Pacific-Biosciences-Template-Preparation-and-Sequencing.pdf (2015)	1019
Tsai	US 2016/0208241 A1, published July 21, 2016	1020

In addition to these references, Petitioner relies on a Declaration of Christophe Dessimoz, Ph.D. (Ex. 1002, “Dessimoz Decl.”).

² The reference indicates that it was published online on May 9, 2010, ahead of its June 2010 print publication date. Under either date, Flusberg is prior art to the challenged claims, which have an earliest possible effective date of August 16, 2019. Ex. 1001, code (60).

F. The Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

Claim(s) Challenged	35 U.S.C. §	Basis
1, 2, 7, 10–12, 14–15, 17–19	103 ³	Flusberg, Flusberg '338, PacBio-BAM
3–6, 9	103	Flusberg, Flusberg '338, PacBio-BAM, Clement
8, 15, 16	103	Flusberg, Flusberg '338, PacBio-BAM, Template Guide
13, 15, 16	103	Flusberg, Flusberg '338, PacBio-BAM, Tsai

Pet. 26.

II. ANALYSIS

A. Claim Construction

The challenged claims should be read in light of the specification, as it would be interpreted by one of ordinary skill in the art. *In re Suitco Surface, Inc.*, 603 F.3d 1255, 1260 (Fed. Cir. 2010). Thus, we generally give claim terms their ordinary and customary meaning. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007) (“The ordinary and customary meaning is the meaning that the term would have to a person of ordinary skill in the art in question.” (internal quotation marks omitted)); *see also*

³ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, which was enacted September 16, 2011, amended 35 U.S.C. § 103. AIA § 3(c). That amendment became effective eighteen months later on March 16, 2013. *Id.* at § 3(n). Because the earliest effective filing date of the claims of the ’794 patent is after March 16, 2013, any citations herein to 35 U.S.C. § 103 are to its AIA version. *Id.* at § 3(n)(1); Ex. 1001, code (60) (listing related applications, the earliest filed of which was filed on August 16, 2019).

37 C.F.R. § 42.100(b) (stating that claims are construed in IPRs according to the same standard as used in federal court).

Neither party proposes an express construction of any term of claim 1. Pet. 27; Prelim. Resp. 10. Nor do we discern a need to provide an express construction of any term of claim 1.

Beyond claim 1, Petitioner argues that certain terms of some of the dependent claims are defined in the '794 patent. *See, e.g.*, Pet. 27 (citing Ex. 1001, 14:65–15:5 as providing a definition for the term “classification”). The Preliminary Response, however, does not contain any argument concerning a dependent claim apart from its dependence from claim 1. *See, e.g.*, Prelim. Resp. 1 (“Because all other asserted Grounds rely upon prevailing on Ground 1 for claim 1, all other grounds fail for the same reasons.”). Thus, we discern no need to provide an express construction of any term of any dependent claim.

B. Obviousness Generally

A claim is unpatentable “if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.” 35 U.S.C. § 103. “Obviousness is a question of law based on underlying facts.” *MobileMedia Ideas LLC v. Apple Inc.*, 780 F.3d 1159, 1167 (Fed. Cir. 2015). The underlying facts include “(i) the scope and content of the prior art, (ii) the differences between the prior art and the claimed invention, (iii) the level of ordinary skill in the field of the invention, and (iv) any relevant objective considerations of

nonobviousness.” *Id.* (citing *Graham v. John Deere of Kan. City*, 383 U.S. 1, 17–18 (1966)). An additional underlying fact is whether there was a reason to combine prior art teachings when so asserted. *Id.*; see also *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418–19 (2007) (“[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.”).

C. Level of Ordinary Skill in the Art

In determining whether an invention would have been obvious at the time it was made, we consider the level of ordinary skill in the pertinent art at the time of the invention. *Graham*, 383 U.S. at 17. “The importance of resolving the level of ordinary skill in the art lies in the necessity of maintaining objectivity in the obviousness inquiry.” *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991). The “person having ordinary skill in the art” is a hypothetical construct, from whose vantage point obviousness is assessed. *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

Petitioner contends a person of ordinary skill in the art of the ’794 patent “would typically have a M.S. or Ph.D. degree with 2-4 years of research experience in genomics, bioinformatics, computational biology, or a related field, or could have less education but significant professional experience in one or more of these fields.” Pet. 26 (citing Ex. 1002 ¶¶74–

75). At this stage of the proceeding, Patent Owner does not dispute Petitioner’s description of a person of ordinary skill in the art or provide its own description. See Prelim. Resp. 10 (“For the purposes of this response, Patent Owner has applied Petitioner’s definition of a person of ordinary skill in the art.”).

Because Petitioner’s formulation of the level of ordinary skill in the art appears consistent with the ’794 patent and the asserted prior art, and because there is no argument to the contrary at this stage of the proceeding, we apply it in our analysis below.

D. Prior Art

1. Flusberg (Ex. 1006)

Flusberg is an article titled “Direct detection of DNA methylation during single-molecule, real-time sequencing,” and was published in 2010.⁴ It is prior art to the challenged claims under 35 U.S.C. § 102(a)(1).

Like the ’794 patent, Flusberg “describe[s] the direct detection of DNA methylation, without bisulfite conversion, through single-molecule, real-time (SMRT) sequencing.” Ex. 1006, Abstract; *see also* Ex. 1001, 2:28–31 (“[T]here is a need to determine the modification of bases of nucleic acids, without prior chemical (e.g. bisulfite conversion) and nucleic acid amplification (e.g. using the PCR).”). “In SMRT sequencing, DNA polymerases catalyze the incorporation of fluorescently labeled nucleotides

⁴ Flusberg indicates that it was published online on May 9, 2010, ahead of a June 2010 print publication date. Under either of those dates, Flusberg is prior art to the challenged claims, which have an earliest possible effective filing date of August 16, 2019. Ex. 1001, code (60).

into complementary nucleic acid strands.” Ex. 1006, Abstract. Flusberg explains that methylation can be detected, in part, by observing and analyzing “polymerase kinetics” based on the “arrival times and duration of the resulting fluorescence pulses.” *Id.*

2. Flusberg ’338 (Ex. 1007)

Flusberg ’338 is a patent titled “Methods For Identifying Nucleic Acid Modifications,” which was filed November 12, 2010 and issued November 3, 2015. Ex. 1007, codes (54), (22), (45). It is prior art to the challenged claims under 35 U.S.C. § 102(a)(1) and (2).

Flusberg ’338 has a disclosure similar to that of Flusberg. Indeed, Patent Owner concedes that both Flusberg and Flusberg ’338 “teach detecting modifications of a nucleotide in a nucleic molecule” by “performing single molecule, real time (SMRT) sequencing of a sample of a nucleic acid molecule and obtaining data for” the “identify of nucleotide,” the “position of the nucleotide, the “width of the pulse corresponding to each nucleotide” and the “interpulse duration (IPD).” Prelim. Resp. 15–16 (quoting Ex. 1004, 803, 806).⁵

3. PacBio-BAM (Ex. 1011)

PacBio-BAM specifies a format for a “BAM file,” in which data obtained from SMRT sequencing can be stored. *See* Ex. 1011, 1 (“The BAM format is a binary, compressed, record-oriented container format for raw or aligned sequence reads.”); Prelim. Resp. 15 (“As Petitioner’s own expert explains, ‘a BAM file is an industry standard file format’ (EX2002,

⁵ Exhibit 1004 is the file history for the ’794 patent.

¶52), and the PacBio-BAM is simply ‘the standard data structure in which PacBio SMRT sequencers store data’ (EX1002, ¶81) that is ‘generated in the normal course of SMRT sequencing’ (EX1002, ¶52).”). PacBio-BAM was published by Petitioner “on its website on or before September 16, 2017.” Pet. 12; *see also* Ex. 1040 (declaration from Nathaniel E. Frank-White, a records request processor at the Internet Archive, citing “Exhibit A” and testifying that it is a screenshot of <http://pacbiofileformats.readthedocs.io/en/5.0/BAM.html> as captured on September 6, 2017); *compare* Ex. 1011, with Ex. 1040, “Exhibit A”). It is prior art to the challenged claims under 35 U.S.C. § 102(a)(1).

E. Discretion Under 35 U.S.C. § 325(d)

Section 325(d) provides, in pertinent part here, that “[i]n determining whether to institute [an inter partes review among other proceedings], the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.” 35 U.S.C. § 325(d). As stated above, the decision whether to institute has been delegated to the Board. 37 C.F.R. § 42.4(a). Patent Owner argues the Board should exercise its discretion under 35 U.S.C. § 325(d) and deny institution under *Advanced Bionics, LLC v. Med-El Elektromedizinische Geräte GmbH*, No. IPR2019-01469, Paper 6 (Feb. 13, 2020) (precedential). Prelim. Resp. 11–26.

In assessing whether to exercise the Board’s authority to deny institution under § 325(d), the Board considers a two-part analysis. *Advanced Bionics* at 8–9. First, the Board considers whether “the same or substantially the same” art or arguments were previously presented to the

Office. *Id.* at 8. If so, the Board then considers whether the petition demonstrates that the Office “erred in a manner material to the patentability of the challenged claims.” *Id.* In applying the two-part framework, the Board considers several nonexclusive factors set forth in *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, No. IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first paragraph).

Patent Owner points out that both Flusberg and Flusberg ’338 were before the Examiner during prosecution. In fact, as Patent Owner argues, both “were expressly relied upon by the examiner” in setting forth rejections under 35 U.S.C. §§ 102 and 103. Prelim Resp. 14 (citing Ex. 1004, 803–810). Patent Owner further points out that Flusberg and Flusberg ’338 were “discussed in an examiner interview.” *Id.* (citing Ex. 1004, 217). After the referenced interview, Patent Owner amended claim 1 and explained Patent Owner’s view that, as amended, claim 1 was patentable over both Flusberg and Flusberg ’338. Ex. 1004, 206–209. The Examiner then allowed claim 1 with no further discussion. Ex. 1004, 174–178. In view of this prosecution history, Flusberg and Flusberg ’338 were clearly before the Examiner.

Patent Owner concedes that PacBio-BAM was not before the Examiner. Prelim. Resp. 15. However, according to Patent Owner, “PacBio-BAM . . . is cumulative to the disclosure of Flusberg and the ’338 patent and adds nothing to the patentability determination here.” *Id.* Patent Owner explains, citing the testimony of Petitioner’s own witness, that “‘a BAM file is an industry standard file format’ (EX2002, ¶52), and the PacBio-BAM is simply ‘the standard data structure in which PacBio SMRT sequencers store data’ (EX1002, ¶81) that is ‘generated in the normal course of SMRT sequencing’ (EX1002, ¶52).” *Id.*

Patent Owner argues that PacBio-BAM is cumulative also in view of the fact that Flusberg '338 discloses that its systems “typically include information processors or computers operably coupled to the detection portions of the systems, in order to store the signal data obtained from the detector(s) on a computer readable medium” and which include “software that analyzes the raw signal data, identifies signal pulses that are likely associated with incorporation events, and identifies bases incorporated during the sequencing reaction, in order to convert or transform the raw signal data into user interpretable sequence data.” Ex. 1007, 71:49–53, 71:62–67; *see* Prelim. Resp. 16–17 (citing the same).

We are not persuaded by Patent Owner’s argument that PacBio-BAM was effectively before the Examiner because it is merely cumulative of other information that was before the Examiner. As Patent Owner argues, “[p]atentability of claim 1 over those same references was further discussed in an examiner interview. EX1004, 217. Then, in response to the rejection, Patent Owner amended claim 1, explaining that claim 1 is patentable over Flusberg and the '338 patent. EX1004, 206–209.” Prelim. Resp. 14. Petitioner relies on PacBio-BAM for teaching or rendering obvious subject matter added to claim 1 by amendment to overcome the rejections based on Flusberg and Flusberg '338. *See* Pet. 39 (“PacBio-BAM teaches creating an input data structure (a BAM file), which, as discussed below, contains each of the recited properties for a window of nucleotides.”), 20 (“PacBio-BAM . . . discloses storing values for PW and IPD.” (citing Ex. 1011, 4–5, 8); Ex. 1011, 8 (stating that “[i]nterpulse duration (IPD) and pulsewidth are measured in frames; . . . recorded[, and] may be encoded in BAM read

tags.”). Patent Owner has not shown, for example, that Flusberg or Flusberg ’338 teach a BAM file having IPD and PW.

Patent Owner does not dispute, and we agree, that Flusberg and Flusberg ’338 disclose or render obvious much of the subject matter of claim 1, including the creating and inputting of an input data structure. *See* Prelim. Resp. 26–45. Patent Owner disputes that Flusberg and Flusberg ’338 disclose or render obvious the particular input data structure recited in claim 1. Indeed, the version of claim 1 that was rejected by the Examiner as anticipated by Flusberg and as obvious over Flusberg ’338 recited “an input data structure.” *See* Ex. 1004, 803 (anticipation rejection), 805 (obviousness rejection), 191 (amendment showing that claim 1 recited “an input data structure” both before and after the amendment). After those rejections, claim 1 was amended in a manner that narrowed the input data structure, by adding the following claim language, which appears in issued claim 1:

(b) creating an input data structure, the input data structure comprising a window of the nucleotides sequenced in the sample nucleic acid molecule, wherein the input data structure includes, for each nucleotide within the window, the properties:

the identity of the nucleotide,
a position of the nucleotide with respect to a target position within the window,
the width of the pulse corresponding to the nucleotide,
and
the interpulse duration.

Ex. 1004, 191; *see also* Ex. 1001, 115:53–63 (same language appearing in issued claim 1). Further, Patent Owner acknowledges and appears to rely on the Examiner’s statement that, “while ‘Flusberg displays various widths of pulses in their sequence window,’ Flusberg does not appear to ‘measure the

widths as a data point to be combined with interpulse duration, nucleotide identity and position in determining the presence of a mutation.” Prelim. Resp. 20 (citing Ex. 1004, 217).

Because PacBio-BAM was not before the Examiner during prosecution and Petitioner relies on PacBio-BAM to address subject matter added to issued claim 1 that the Examiner presumably found to be lacking in Flusberg and Flusberg ’338, we are not persuaded that PacBio-BAM is merely cumulative of other information that was before the Examiner as Patent Owner argues. Whether Petitioner might ultimately prove by a preponderance of evidence on a fully developed record at trial that claim 1 (and other claims) would have been obvious over Flusberg, Flusberg ’338, and PacBio-BAM remains to be seen. Under these circumstances, we determine that we should not discretionarily deny institution under 35 U.S.C. § 325(d) because we find that the same or substantially prior art was not previously presented to the Office.

F. Analysis of Challenge to Claim 1

Petitioner contends that claim 1 is unpatentable under 35 U.S.C. § 103 because it would have been obvious over Flusberg, Flusberg ’338, and PacBio-BAM.

1. Input Data Structure

As discussed above, it appears the main dispute between the parties about the *scope* of the combined prior art and thus the difference between it and the claimed invention is whether Flusberg, Flusberg ’338, and PacBio-BAM render obvious an input data structure as recited in claim 1. Patent Owner repeatedly emphasizes that the Examiner found no prior art that

discloses an input data structure having the specific combination of properties listed in claim 1. More specifically, Patent Owner argues:

the examiner recognized that despite using the data generated in the normal course of SMRT sequencing (EX1004, 803, 806), Flusberg and the '338 patent do not appear to “measure the widths as a data point to be combined with interpulse duration, nucleotide identity and position in determining the presence of a mutation.” EX1004, 217. In other words, *neither reference discloses the combination of features of the “input data structure” in claim 1.*

Prelim. Resp. 2 (emphasis added).

During prosecution the Examiner allowed claim 1 over Flusberg and the '338 patent, finding that while “Flusberg displays various widths of pulses in their sequence data in a window,” Flusberg does not appear to “measure the widths as a data point to be combined with interpulse duration, nucleotide identity and position in determining the presence of a mutation.” EX1004, 217. The examiner references that same conclusion with respect the '338 patent. *Id.* In other words, while Flusberg and the '338 patent both disclose receiving the standard output of SMRT sequencing, claim 1 is patentable over those references because *the references do not disclose using that standard output of SMRT sequencing to create an “input data structure” having the claimed combination of features including pulse width, interpulse duration, nucleotide identify and position to determine the presence of a mutation.*

Id. at 12–13 (emphasis added).

Specifically, following an interview discussing the proposed claim amendments and Flusberg and the '338 patent, the examiner stated that while “Flusberg displays various widths of pulses in their sequence window,” *Flusberg does not appear to “measure the widths as a data point to be combined with interpulse duration, nucleotide identity and position in determining the presence of a mutation.”* EX1004, 217.

Id. at 20 (emphasis added); *see also id.* at 23 (almost identical statement).

Here, the Board should not second guess the Examiner's determination that Flusberg and the '338 patent *do not disclose "measur[ing] the widths as a data point to be combined with interpulse duration, nucleotide identity and position in determining the presence of a mutation"* and thus do not render obvious claim 1. EX1004, 217.

Id. at 28 (emphasis added).

Petitioner argues that an input data structure having the recited combination of properties would have been obvious, in part, because all such properties were identified and could be measured in the prior art. For example, according to Petitioner, "[i]n addition to encoding the identity and relative locations of each nucleotide, PacBio-BAM encodes the PW and IPD of each nucleotide as integer arrays." Pet. 43 (citing Ex. 1011, 8). This argument is supported by the cited evidence. Under a section titled "Encoding of kinetics pulse features," PacBio-BAM states: "Interpulse duration (IPD) and pulsewidth are measured in frames [and] . . . may be encoded in BAM read tags" and further states such information relates to "base modification detection." Ex. 1011, 8. Petitioner also notes that Flusberg and Flusberg '338 teach that PW and IPD are affected by nucleotide modifications. Pet. 43–44 (citing Ex. 1007, 66:46–67:4, 9:41–46; 22:49–54; Figs. 12, 13, and 15–19; Ex. 1006, 462, Fig. 3). For example, Flusberg '338 teaches:

In certain aspects, the invention provides a general-purpose approach to discriminating between Me⁺ and Me⁻ using features in a real-time sequencing-by-synthesis trace comprising signals emitted during the incorporation of optically detectable nucleotides into a nascent strand by a polymerase enzyme. . . . A first stage of this approach includes the development of a classifier for distinguishing methylated from unmethylated cytosines in a nucleic acid template. A set of features is measured for every pulse (discrete event or signal) in the trace.

For example, *a set of measurable features might be {pulse width, pulse duration, pulse height, pulse amplitude variability}*.

Ex. 1007, 64:46–59 (emphasis added). Similarly, Flusberg states:

Fluorescence pulses in SMRT sequencing are characterized not only by their emission spectra but also by their duration and by the interval between successive pulses. *These metrics, defined here as pulse width and interpulse duration (IPD), add valuable information about DNA polymerase kinetics.* Pulse width is a function of all kinetic steps after nucleotide binding and up to fluorophore release, and IPD is determined by the kinetics of nucleotide binding and polymerase translocation. We have previously demonstrated that SMRT sequencing polymerase synthesis rates are sensitive to DNA primary and secondary structure. Therefore, we hypothesized that methylated bases in a DNA template might be detected directly on the principle that their presence affects polymerase kinetics during SMRT sequencing.

Ex. 1006, 462 (emphasis added; end notes omitted).

Petitioner argues that “PacBio-BAM teaches creating an input data structure (a BAM file),” of SMRT data regarding measured properties and that the prior art, including PacBio-BAM itself, teaches each of the properties recited in the claim. Pet. 39. Relying on the testimony of Dr. Dessimoz, Petitioner argues that a person of ordinary skill in the art “would have found it obvious to consider the claimed properties together because doing so represents nothing beyond the predictable use of known variables according to their well-characterized role in base modification detection.” Pet. 31 (citing Ex. 1002 ¶¶83–84); see *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2017) (“[A] court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.”). Petitioner also argues that there would have been a reasonable expectation of success because it merely involves adding PW data to the

input data structure, which PW data was already being generated in the prior art SMRT sequencing. Pet. 32; *see also* Prelim. Resp. 30 (acknowledging that “a POSITA would understand that . . . the PacBio-BAM includes information from which the input data structure could be created”).

Patent Owner argues that PacBio-BAM is not the recited “input data structure,” but rather “is simply the digital form of the SMRT sequencing data which is ‘generated in the normal course of SMRT sequencing.’” Prelim. Resp. 31 (quoting Ex. 1002 ¶52). This argument, however, does not rebut Petitioner’s position. Petitioner does not argue that PacBio-BAM explicitly teaches an input data structure containing all four of the recited properties (i.e., identity, relative position, PW, and IPD) for each nucleotide in the window. Petitioner argues, rather, that PacBio-BAM teaches an input data structure containing properties measured during SMRT sequencing, the prior art discloses all four of the properties recited in the claim, and it would have been obvious to combine all four in an input data structure. Pet. 31, 39.

Patent Owner argues that a BAM file, as taught by PacBio-BAM, is a compressed binary format that “cannot be read by a machine leaning [sic] model and comprises text data, not an input data array necessary for training a model” and thus its “storage format is incompatible as input data structure for training a model.” Prelim. Resp. 31 (citing Ex. 2002 ¶126; Ex. 1011, 1). This argument is not persuasive. First, the prosecution history suggests that Flusberg and Flusberg ’338 each teach or render obvious an input data structure, albeit not one having all of four properties recited in claim 1. This is suggested in the prosecution history because the Examiner’s rejections over Flusberg and Flusberg ’338 were overcome by Patent Owner, not by argument, but by narrowing the input data structure to require the

combination of the four properties recited in claim 1. Second, in its infringement contentions in the related lawsuit, Patent Owner itself contends that an allegedly infringing “input data structure is created from the data in the PacBio-BAM.” Prelim. Resp. 2; *see also* Ex. 1014, 25 (“The HiFi reads in the BAM file are then used to create the data structure of the claimed element [1.b], i.e., an input data structure, for claim element [1.c].”).⁶ Yet, Patent Owner does not explain why a person of ordinary skill in the art could not have done so using the substantively identical teaching in the asserted PacBio-BAM.⁷ Third, we are not persuaded by Patent Owner’s implication that a skilled artisan would thoughtlessly incorporate “text data” that would sabotage the utility of an input data structure, as Patent Owner suggests would occur. Prelim. Resp. 31; *see KSR Int’l*, 550 U.S. at 421 (“A person of ordinary skill is also a person of ordinary creativity, not an automaton.”).

In sum, we find that, on the current record, Petitioner has sufficiently shown a reasonable likelihood that Flusberg, Flusberg ’338, and PacBio-BAM render obvious an input data structure as recited in claim 1.

2. Target Position

Claim 1 recites: “(d) determining, using the model, whether the modification is present in a nucleotide at the target position within the window in the input data structure.” Patent Owner argues that PacBio-BAM

⁶ Exhibit 1014 is an infringement claim chart Patent Owner real party in interest, Take2 Technologies Limited, filed in the related lawsuit.

⁷ According to Petitioner, and not disputed by Patent Owner, the PacBio-BAM referenced in Patent Owner’s infringement contentions is “a later version” of the PacBio-BAM reference asserted in the Petition but is “substantively identical.” Pet. 20.

does not teach a “‘target position within a window’ let alone ‘a position of the nucleotide with respect to a target position within the window’ as required by claim 1.” Prelim. Resp. 32. The gist of Patent Owner’s argument is that PacBio-BAM uses the word “target” to mean something other than that word’s meaning in the claim. *Id.* at 32–33. Yet, Patent Owner declines to propose an express construction for “target” or “target window.” *Id.* at 10, 32–33. Nor is the purported distinction apparent based on the plain and ordinary meaning. As such, the argument is not persuasive.

In any event, the Petition does not rely exclusively, or even primarily, on PacBio-BAM for teaching the “target position” limitation. Rather, Petitioner argues that each of Flusberg and Flusberg ’338 teach a “target position” as well as a “window” of nucleotides encompassing the target position. For example, Petitioner argues the following:

Flusberg-338’s feature vector labels each nucleotide’s set of features with a superscript indicating its relative position, with superscript i representing the target nucleotide’s pulse, and the other nucleotides being labeled from $i-3$ to $i+3$. EX1007, 66:46-67:4. These labels are direct indications of each nucleotide’s position with respect to the target position (nucleotide i) within the window. EX1002, ¶114. . . .

Like Flusberg-338, Flusberg describes that each weight is identified with a particular nucleotide based on its position relative to the nucleotide of interest, identified as nucleotide 0. See EX1006, 478; EX1002, ¶115.

Pet. 41–42; *see also id.* at 38 (“Dr. Dessimoz explains [with respect to Flusberg ’338], the resulting feature vector is a ‘data structure comprising a window of the nucleotides sequenced in the sample nucleic acid molecule,’ corresponding to the claimed ‘input data structure’ at least because the feature vector is an input for a model that distinguishes methylated and

unmethylated nucleotides.” (citing Ex. 1002 ¶¶103–104)). Patent Owner’s Preliminary Response fails to address, let alone rebut, these arguments, which are supported by the evidence Petitioner cites.

3. The Model Trained By . . .

Claim 1 recites “the model trained by: receiving a first plurality of first data structures, . . . each first data structure comprising values for the same properties as the input data structure.” Petitioner argues that Flusberg ’338 teaches such a model in the form of a “a classifier for distinguishing methylated from unmethylated cytosines in a nucleic acid template.” Ex. 1007, 66:55–57; *see also* Pet. 44 (quoting the same). Petitioner adds that “Flusberg-338 discloses that this ‘general classifier . . . can be implemented with many standard statistical classification algorithms, i.e. linear discriminant analysis, multi-dimensional regression, kernel methods, classification and regression trees, neural networks, and support vector machines.’” Pet. 45 (quoting Ex. 1007, 67:6[7]–68:5). Petitioner argues that Flusberg teaches a similarly trained model. Pet. 46 (citing Ex. 1006, 463; Ex. 1002 ¶¶125–127).

Patent Owner argues that “sequence data in the format of the PacBio-BAM is of varying lengths, and thus cannot be used to train a model as required by claim 1.” Prelim. Resp. 33 (citing Ex. 2002 ¶128). This argument is similar to Patent Owner’s unpersuasive argument, discussed above, that PacBio-BAM’s storage format is incompatible with it serving as an input data structure for training a model. Prelim. Resp. 31. The instant argument likewise is not persuasive on the present record.

As discussed above, Patent Owner itself contends that an allegedly infringing “input data structure is created from the data in the PacBio-BAM.” Prelim. Resp. 2; *see also* Ex. 1014, 25 (“The HiFi reads in the BAM file are then used to create the data structure of the claimed element [1.b], i.e., an input data structure, for claim element [1.c].”). Yet, as also discussed above, Patent Owner does not explain why a person of ordinary skill in the art could not have done so using the substantively identical teaching in the asserted PacBio-BAM and used it to train a model. Similarly, Patent Owner also has not shown why a skilled artisan would thoughtlessly fail to address any incompatibilities in the data structure. *See KSR Int’l*, 550 U.S. at 421 (“A person of ordinary skill is also a person of ordinary creativity, not an automaton.”).

4. Reason To Combine

Petitioner points out that (1) each of Flusberg and Flusberg ’338 teach methods of detecting nucleotide modifications using SMRT sequencing, and (2) PacBio-BAM teaches a BAM file containing values for all claimed properties generated in the course of SMRT sequencing. Pet. 29. Petitioner argues with supporting evidence, that it would have been obvious “to use PacBio’s BAM file containing the recited properties as an input data structure, as expressly suggested in PacBio-BAM.” *Id.* at 29–30; *see also* Ex. 1002 ¶82 (Dr. Dessimoz providing his opinion in support of the combination); Pet. 30–33 (providing additional arguments and evidence to support the combination).

Patent Owner argues that “Petitioner fails to provide motivation to combine Flusberg with the other two references of Ground 1 to arrive at the

claimed invention.” Prelim. Resp. 45. According to Patent Owner, “Petitioner makes no argument for why Flusberg and the ’338 patent would be combined, let alone why a POSITA would selectively combine various aspects of each reference and include features not used in either reference to arrive.” *Id.* Patent Owner premises its argument on a purported failure by Flusberg ’338 to incorporate by reference the entire Flusberg reference as opposed to limited aspects of its. *Id.* at 45–46.

Flusberg ’338 patent twice states that Flusberg is “incorporated herein by reference in its entirety for all purposes.” Ex. 1007, 77:30–24, 78:58–66. Patent Owner argues that what is incorporated by reference is only the specific content of Flusberg that is mentioned by Flusberg ’338. Prelim. Resp. 46. Patent Owner cites *Nautilus, Inc. v. Icon Health & Fitness Inc.*, No. IPR2017-01407, 2018 WL 6321395, at *18–19 (PTAB Dec. 3, 2018) in support. *Id.* Patent Owner additionally points out that, if either incorporation by reference successfully incorporated the entire Flusberg disclosure, then the other incorporation by reference would be superfluous. Prelim. Resp. 46–47. This last point is logical, but the totality of the facts, as discussed below, better support Petitioner’s position.

In *Nautilus*, the Board interpreted the following incorporation by reference language: “The ’088 Application provides ‘One example of customizing a work-out that may be utilized in conjunction with the exercise apparatus described herein is set forth in U.S. Patent Application No. 13/754,361, filed on Jan. 30, 2013, the disclosure of which is incorporated by reference herein in its entirety.’” *Nautilus*, 2018 WL 6321395, at *19. The Board found that the word “disclosure” could refer to either the example being discussed or the entire disclosure of the ’088 Application, and the

Board ultimately held that what was incorporated by reference was the example of customizing a work-out only and not the entirety of the '088 Application. *Id.* *Nautilus* is not precedential. Moreover, its facts are different. Here, we have statements that Flusberg is incorporated by reference both “in its entirety” and “for all purposes.” Ex. 1007, 77:30–24, 78:58–66.

Further, the Board’s holding in *Nautilus* explicitly hinged on its understanding of the word “disclosure” in the following phrase: “the disclosure of which is incorporated by reference herein in its entirety.” *Nautilus*, 2018 WL 6321395, at *19. The Board held that, “as a matter of grammar, the antecedent of the ‘disclosure’ being incorporated could be either the application or ‘one example’ that is described in the application.” *Id.* Here, the rules of grammar contradict Patent Owner’s position, rather than support it. For example, the first incorporation by reference states: “Further details on the detection of N⁶-MeA, as well as other modifications within a template nucleic acid, are provided in Flusberg, et al. (2010) Nature Methods 7(6):461–465, incorporated herein by reference in *its entirety* for all purposes.” Ex. 1007, 77:30–24 (emphasis added). The word “its” can refer to only one thing, Flusberg itself, as the alternative would be plural nouns, namely “details” and “other modifications,” and thus inconsistent with the singular “its.”

In sum, we find that, on the current record, Petitioner has sufficiently shown a motivation to combine Flusberg and Flusberg ’338 with PacBio-BAM.

5. *Objective Indicia*

Under 35 U.S.C. § 103, “the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved.” *Graham*, 383 U.S. at 17. However, objective indicia, also known as secondary considerations, “may have relevancy” to obviousness or nonobviousness of claimed subject matter. *Id.* at 17–18.

Objective indicia evidence “must always be considered when present en route to a determination of obviousness.” *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983). However, “to be accorded substantial weight in the obviousness analysis, the evidence of secondary considerations must have a ‘nexus’ to the claims, i.e., there must be ‘a legally and factually sufficient connection’ between the evidence and the patented invention.” *Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1332 (Fed. Cir. 2019). Patent Owner bears the burden of proving nexus. *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (“For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention.”); *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988) (“The burden of proof as to this connection or nexus resides with the patentee.”).

Nexus can be established in one of two ways. First, “a patentee is entitled to a rebuttable presumption of nexus between the asserted evidence of secondary considerations and a patent claim if the patentee shows that the asserted evidence is tied to a specific product and that the product ‘is the invention disclosed and claimed.’” *Fox Factory, Inc. v. SRAM, LLC*, 944

F.3d 1366, 1373 (Fed. Cir. 2019) (quoting *Demaco*, 851 F.2d at 1392). “That is, presuming nexus is appropriate ‘when the patentee shows that the asserted objective evidence is tied to a specific product and that product [1] ‘embodies the claimed features, and [2] is coextensive with them.’” *Id.* (quoting *Polaris Indus., Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1072 (Fed. Cir. 2018)); *see also Fox Factory, Inc. v. SRAM, LLC*, 813 F. App’x 539, 542, 2020 WL 2517105 (Fed. Cir. 2020) (“[A] product is not coextensive with a claimed invention simply because it falls within the scope of the claim.”).

The second way to prove nexus is directly, by showing that the presented evidence of secondary considerations is “a direct result of the unique characteristics of the claimed invention.” *In re Huang*, 100 F.3d 135, 140 (Fed. Cir. 1996); *Fox Factory*, 944 F.3d at 1373–74 (Absent a presumption, nexus can be proved “by showing that the evidence of secondary considerations is the direct result of the unique characteristics of the claimed invention.”).

a) Unexpected Results

“To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention.” *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014).

Patent Owner argues that (1) it was “unexpected” that “the predictive power of PW is greater than IPD” and (2) its “combination of features that make up the input data structure of claim 1” was a significant improvement and unexpected over the closest prior art. Prelim. Resp. at 48

As for Patent Owner's first point, there is a clear lack of nexus between the purported unexpected result (predictive power of PW alone being greater than IPD alone) and the claimed invention, which requires both PW and IPD.

As for Patent Owner's second point, Patent Owner fails to show that the observed improvement from combining the properties would have been unexpected.

Figures 18A and 18B of the '794 patent are reproduced below with coloring added by Patent Owner.

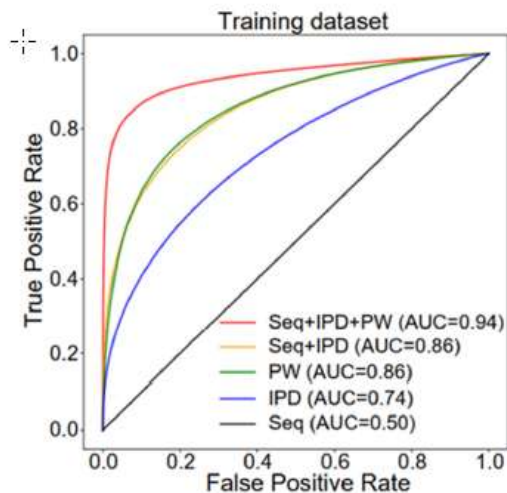


FIG. 18A

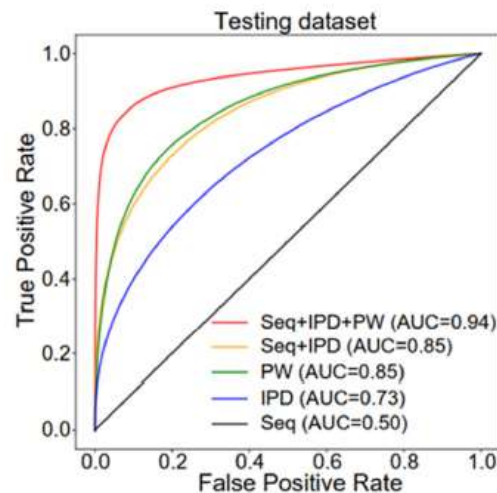


FIG. 18B

Ex. 2001, Figs. 18A and 18B.⁸ Figures 18A and 18B of the '794, reproduced above with coloring added, “show the performance of a training dataset and a testing dataset for determining methylation according to embodiments of the present invention.” Ex. 1001, 4:34–36. Referring to Figure 18A in particular, the '794 patent explains that “combining IPD and

⁸ Exhibit 2001 is a colored copy of the '794 patent Figures. *Compare, e.g.,* Ex. 1001, Figs. 18A–B, *with* Ex. 2001, Figs. 18A–B.

sequence context improved the performance with an AUC [(i.e., area-under-the-curve)] of 0.86” but that “[t]he combined analysis of sequence context (‘Seq’), IPD, and PW substantially improved the performance with an AUC of 0.94 (FIG. 18A).” *Id.* at 32:24–27. Patent Owner argues that the improvement from 0.86 to 0.94 when adding PW to the combination of properties constitutes unexpected results over the closest prior art. Prelim. Resp. 48.

Adding PW to the combination may be a “substantial[] improve[ment]” as asserted in the ’794 patent, but Patent Owner has not established that the identified improvement would have been unexpected over the closest prior art. Flusberg explicitly teaches the following:

Fluorescence pulses in SMRT sequencing are characterized not only by their emission spectra but also by their duration and by the interval between successive pulses. *These metrics, defined here as pulse width and interpulse duration (IPD), add valuable information about DNA polymerase kinetics.* Pulse width is a function of all kinetic steps after nucleotide binding and up to fluorophore release, and IPD is determined by the kinetics of nucleotide binding and polymerase translocation.

Ex. 1006, 462 (emphasis added). Similarly, Flusberg ’338 teaches that “the presence of modified bases in a template nucleic acid has been shown to change the width of a pulse and/or the interpulse duration (IPD), either at the modified base or at one or more positions proximal to it.” Ex. 1007, 22:49–52. Thus, both Flusberg and Flusberg ’338 teach that PW is affected by nucleotide modification, with Flusberg explicitly stating that PW “add[s] valuable information.” Ex. 1006, 462. In other words, these teachings suggest to the person of ordinary skill in the art that incorporating PW into a detection analysis would improve the analysis, i.e., that the person of ordinary skill would have expected an improvement.

To the extent Patent Owner relies on the *degree* of improvement to demonstrate unexpected results, Patent Owner fails to provide sufficient context to support such an argument. In that regard, Patent Owner merely labels the improvement identified in the '794 patent (i.e., 0.94 AUC versus 0.86 AUC) as “significant[]” and equates that with unexpected. Prelim. Resp. 48. Similarly, Patent Owner’s witness, Peter K. Koo, PhD., summarily labels the improvement as “unpredicted,” which is not the standard. Ex. 2002 ¶143.

Patent Owner provides no context for one to determine that the improvement was unexpected. In particular, Patent Owner makes no showing about what a person of ordinary skill in the art allegedly would have expected by adding PW to the combination of properties, which is required in order to properly evaluate an unexpected results argument. *See Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1371 (Fed. Cir. 2007) (“[B]y definition, any superior property must be unexpected to be considered evidence of non-obviousness. Thus, in order to properly evaluate whether a superior property was unexpected, the [fact-finder] should have considered what properties were expected. Here, Pfizer’s evidence must fail because the record is devoid of any evidence of what the skilled artisan would have expected.”).

Patent Owner does state that a person of ordinary skill “would [have] expect[ed] that IPD would have [had] more predictive power than PW in detecting base modifications,” but fails to identify, let alone show, what the skilled artisan would have expected by combining PW and IPD along with the other two properties recited in the claim. Prelim. Resp. 47; *see also* Ex. 2002 ¶143 (An unexpected result of the '794 patent is the predictive

power of PW as a feature which had a 0.85 AUC compared to 0.73 AUC for IPD.”).

b) Long Felt But Unresolved Need

Patent Owner argues that, although “Flusberg discloses that it might be possible to detect modifications, . . . three years after Flusberg and the ’338 patent, no actual method of doing so had been proposed.” Prelim. Resp. 52. Even assuming three years is a long time given the context, Patent Owner’s argument does not address adequately the unresolved/unsolved need component of the secondary consideration being asserted. *See Monarch Knitting Machinery Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 884 (Fed. Cir. 1998) (“The relevant secondary consideration is ‘long-felt *but unsolved need*,’ not long-felt need in isolation.”). More specifically, Patent Owner does not identify any previous but failed attempts to solve the purported problem. *See Texas Instruments v. Int’l Trade Comm’n*, 988 F.2d 1165, 1178 (Fed. Cir. 1993) (“[L]ong-felt need is analyzed as of the date of an articulated identified problem *and evidence of efforts to solve that problem*.” (emphasis added)).

c) Petitioner’s Praise

Patent Owner argues that “[t]he nonobviousness of the ’794 patent is further confirmed by Petitioner’s praise for the invention of the ’794 patent as described in Tse (EX 1030).” Prelim. Resp. 53. We have reviewed the statements in question and consider them not strongly probative of non-obviousness.

According to Patent Owner, it “sent the article [(i.e., Tse, Ex. 1030)] to Petitioner to negotiate a collaboration or licensing agreement related to the ’794 patent’s invention.” Prelim. Resp. 53. Patent Owner does not state

whether a collaboration or licensing agreement was successfully negotiated and entered into between Petitioner and Patent Owner. *Id.* Patent Owner does state, however, that “Petitioner then praised the invention.” *Id.*

The identified statements of praise are ambiguous as to whether they are probative of non-obviousness. At least one of the statements suggests that a collaborative relationship between the parties existed at the time of the statements. *See* Prelim. Resp. 53 (“Petitioner’s president and chief executive officer, Christian Henry, praised the invention in a public earnings call stating that he would ‘like to share some customer highlights that really demonstrate the power and potential of PacBio HiFi sequencing technology.’” (citation for quotation not provided by Patent Owner)). Thus, the purported praise of the invention logically could be attributed to Petitioner praising its own business and decision to collaborate or Petitioner praising Patent Owner’s technology for its own pecuniary benefit.⁹

d) Copying

Patent Owner argues that, “[f]ollowing Patent Owner sending Tse to Petitioner, Petitioner then copied the invention of the ’794 patent.” Prelim. Resp. 55. Patent Owner argues that Petitioner’s copying was in the form of “a new version of its SMRT Analysis Software suite—SMRT Link v11.0—including the new feature ‘New data utility to perform 5mC CpG Detection.’” *Id.* (citing Ex. 2028, 2). Patent Owner asserts that portions of Exhibits 2016 and 1014 show how the Petitioner’s new software “infringes

⁹ If Petitioner’s praise of the invention is re-raised at trial, it would be helpful for the Board to know the relationship between the parties at the time each statement was made.

the '794 patent.” *Id.* (citing Ex. 2016 ¶¶34–63; Ex. 1014, 5–50). Patent Owner’s copying position is not persuasive.

The cited paragraphs from Exhibit 2016, which is the public version of Patent Owner’s Complaint filed in the related lawsuit, is argument. The cited portion of Exhibit 1014, which is an infringement claim chart, also contains some argument. We do not consider those arguments placed outside the Preliminary Response. *See* 37 C.F.R. § 42.6(a)(3) (“Arguments must not be incorporated by reference from one document into another document.”). That said, even if we were to assume that Petitioner’s new software “infringes the '794 patent,” as asserted by Patent Owner, copying requires more than infringement. “Not every competing product that arguably falls within the scope of a patent is evidence of copying. . . . Rather, copying requires the replication of a specific product.” *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1325 (Fed. Cir. 2004). Thus, Patent Owner must prove more than mere infringement to establish copying.

G. Conclusion Regarding Claim 1

Petitioner has demonstrated a reasonable likelihood of prevailing on its challenge to claim 1 as unpatentable under 35 U.S.C. § 103 due to obviousness over Flusberg, Flusberg '338, and PacBio-BAM.

H. Remaining Claims of Ground 1 and Grounds 2–4

Patent Owner does not present any arguments specific to any claim beyond claim 1. *See, e.g.*, Prelim. Resp. 1 (“Because all other asserted Grounds rely upon prevailing on Ground 1 for claim 1, all other grounds fail for the same reasons.”). In any event, the threshold for institution is a

reasonable likelihood of Petitioner prevailing as to any single claim. 35 U.S.C. § 314(a). “Once that single claim threshold is satisfied, it doesn’t matter whether the [P]etitioner is likely to prevail on any *additional* claims.” *SAS Institute, Inc. v. Iancu*, 138 S. Ct. 1348, 1356 (2018). Thus, because we have decided to grant review of claim 1, we do the same for all claims challenged and all grounds raised. *Id.*; *see also* 37 C.F.R. § 42.108(a) (“When instituting *inter partes* review, the Board will authorize the review to proceed on all of the challenged claims and on all grounds of unpatentability asserted for each claim.”).

III. CONCLUSION

For the reasons discussed above, we are persuaded that Petitioner has demonstrated a reasonable likelihood of prevailing in establishing that at least one of the challenged claims is unpatentable.

IV. ORDER

In consideration of the foregoing, it is hereby

ORDERED that the Petition is granted and *inter partes* review is hereby instituted as to claims 1–19 of U.S. Patent No. 11,091,794 B2 on the grounds presented; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial on the grounds of unpatentability authorized above; the trial commences on the entry date of this decision.

IPR2024-00028
Patent 11,091,794 B2

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