NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

10X GENOMICS, INC.,
Appellant

v.

PARSE BIOSCIENCES, INC.,
Appellee

2025-1199

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2023-00876.

10X GENOMICS, INC.,
Appellant

v.

PARSE BIOSCIENCES, INC.,
Appellee

2025-1618, 2025-1619

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2023-00955, IPR2023-00958.

Decided: August 19, 2026

THOMAS SAUNDERS, Wilmer Cutler Pickering Hale and Dorr LLP, Washington, DC, argued for appellant. Also represented by GARY M. FOX, OMAR KHAN, New York, NY; BENJAMIN MORRIS, Boston, MA.

EDWARD R. REINES, Jones Day, Palo Alto, CA, argued for appellee. Also represented by CONCORD CHEUNG; DEREK C. WALTER, San Francisco, CA.

Before TARANTO, BRYSON, and CUNNINGHAM, *Circuit Judges*.

CUNNINGHAM, *Circuit Judge*.

10x Genomics ("10x") appeals final written decisions by the Patent Trial and Appeal Board in *inter partes* reviews ("IPRs") brought by Parse Biosciences, Inc. ("Parse"). The Board determined that all claims of U.S. Patent No. 10,155,981 ("the '981 patent"), U.S. Patent No. 10,240,197 ("the '197 patent"), and U.S. Patent No. 10,697,013 ("the '013 patent"), are unpatentable as obvious. *Parse Biosciences, Inc. v. 10x Genomics, Inc.*, No. IPR2023-00876, 2024 WL 4218540, at *1 (P.T.A.B. Sep. 17, 2024) ("*'981 Decision*"); *Parse Biosciences, Inc. v. 10x Genomics, Inc.*, No. IPR2023-00955, 2025 WL 355170, at *1 (P.T.A.B. Jan. 31, 2025) ("*'197 Decision*"); *Parse Biosciences, Inc. v. 10x Genomics, Inc.*, No. IPR2023-00958, 2025 WL 383299, at *1 (P.T.A.B. Feb. 3, 2025) ("*'013 Decision*"). For the reasons below, we *affirm*.

I. BACKGROUND

The patents claim methods for analyzing nucleic acids from single cells. '981 patent col. 30 ll. 19–62; '197 patent col. 30 l. 16 to col. 32 l. 25; '013 patent col. 30 l. 38 to col. 32 l. 59.[1] Claims 1 and 5 of the '981 patent recite:

> 1. A method of analyzing nucleic acids from a plurality of single cells, the method comprising:
>
> (a) providing a sample comprising a plurality of single cells, wherein each single cell of the plurality of single cells comprises a plurality of sample polynucleotides;
>
> (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides, wherein each tagged polynucleotide comprises:
>
> (i) a sequence from a sample polynucleotide of the plurality of sample polynucleotides; and
>
> (ii) a multiplex identifier (MID) sequence comprising:
>
> I. a first tag sequence associated with the single cell from which the sample polynucleotide is derived, wherein the first tag sequence is a different sequence for different single

[1] The '197 patent is a continuation of the '981 patent, and the '013 patent is in the same patent family. All three patents share a specification, and citations to the specification will be to that of the '981 patent.

cells in the plurality of single cells; and

II. a second tag sequence distinguishing the sample polynucleotide from other sample polynucleotides derived from the same single cell;

(c) sequencing the plurality of tagged polynucleotides to obtain a plurality of identified polynucleotide sequences;

(d) *using the first tag sequence to correlate the identified polynucleotide sequence with the single cell* from which the identified polynucleotide sequence is derived; and

(e) *using the second tag sequence to correlate the identified polynucleotide sequence with the sample polynucleotide* from which the identified polynucleotide sequence is derived.

5. The method of claim 1, wherein the tagged polynucleotides are generated through at least one ligation reaction.

'981 patent col. 30 ll. 19–48, 56–57 (emphases added). Claims 1 and 5 of the '197 patent recite:

1. A method of counting nucleic acids in a sample, the method comprising:

(a) providing a sample comprising a plurality of cells, wherein a cell of the plurality of cells comprises a plurality of sample polynucleotides;

> (b) generating a plurality of tagged polynucleotides from the plurality of sample polynucleotides of said cell and a plurality of oligonucleotide tags, wherein a tagged polynucleotide of the plurality of tagged polynucleotides comprises:
>
> > (i) a sample sequence from a sample polynucleotide of the plurality of sample polynucleotides;
> >
> > (ii) a first tag sequence distinguishing said sample polynucleotide from sample polynucleotides from other cells; and
> >
> > (iii) a second tag sequence distinguishing said sample polynucleotide from other sample polynucleotides from said cell;
>
> (c) sequencing the tagged polynucleotide to determine the sample sequence, the first tag sequence, and the second tag sequence; and
>
> (d) using the first tag sequence and the second tag sequence to count a number of sample polynucleotides in said plurality of sample polynucleotides of said cell.
>
> 5. The method of claim 1, wherein the plurality of tagged polynucleotides is generated through *at least one ligation reaction*.

'197 patent col. 30 ll. 16–39, 47–49 (emphasis added). Claim 1 of the '013 patent recites:

> 1. A method for multiplexed analysis of nucleic acids from single cells, the method comprising:

(a) providing a sample comprising a plurality of cells, wherein a single cell of the plurality of cells comprises a plurality of sample polynucleotides;

(b) performing combinatorial tagging to generate a plurality of tagged polynucleotides from said plurality of sample polynucleotides and a plurality of oligonucleotide tags, wherein a tagged polynucleotide of the plurality of tagged polynucleotides is generated by:

(A) providing an extension product by primer extension using a first oligonucleotide tag and a sample polynucleotide of said plurality of sample polynucleotides, and

(B) *ligating a second oligonucleotide tag* to said extension product, and

wherein said tagged polynucleotide of the plurality of tagged polynucleotides comprises:

(i) a sample sequence corresponding to said sample polynucleotide of the plurality of sample polynucleotides;

(ii) a first tag sequence distinguishing said sample polynucleotide from sample polynucleotides from other cells; and

(iii) a second tag sequence distinguishing said sample

> polynucleotide from other sample polynucleotides from said cell;
>
> (c) amplifying said tagged polynucleotide, thereby generating a plurality of amplified polynucleotides corresponding to the tagged polynucleotide; and
>
> (d) sequencing said plurality of amplified polynucleotides to determine sequences of the amplified polynucleotides corresponding to the sample sequence, the first tag sequence, and the second tag sequence of the tagged polynucleotide; and
>
> (e) using the sequences determined in step (d) to count sample polynucleotides for multiple different sample polynucleotides of multiple different single cells of said plurality of cells.

'013 patent col. 30 l. 38 to col. 31 l.9 (emphasis added).

In its final written decisions, the Board determined that all claims of the '981 patent, claims 1–12, 20–26 of the '197 patent, and claims 1–12 and 19–28 of the '013 patent are unpatentable as obvious over the combination of Linnarsson[2] and McCloskey.[3] *'981 Decision* at *23; *'197 Decision* at *32; *'013 Decision* at *23. Additionally, the Board determined that the remaining claims of the '197 and '013 patents are unpatentable as obvious over the combination

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[2] PCT Patent Pub. No. WO 2010/117620 (filed Mar. 30, 2010; published Oct. 14, 2010), 25-1199 J.A. 1119–89 ("Linnarsson").

[3] Megan L. McCloskey et al., *Encoding PCR Products with Batch-stamps and Barcodes*, 45 BIOCHEM GENET 761–67 (2007), 25-1199 J.A. 1190–96 ("McCloskey").

of Linnarsson, McCloskey, and McCloskey II.[4] *'197 Decision* at *32; *'013 Decision* at *23.

The Board found a motivation to combine Linnarsson and McCloskey in all decisions. *'981 Decision* at *14–17; *'197 Decision* at *15–20; *'013 Decision* at *15–19. For all three patent IPRs, the Board also found motivation to combine Linnarsson and McCloskey using ligation as a design choice to improve flexibility. *'981 Decision* at *20–22; *'197 Decision* at *27–28; *'013 Decision* at *16–19. Additionally, for the '981 patent IPR, the Board determined that the combination of Linnarsson and McCloskey discloses the "correlate" limitations of claim 1. *'981 Decision* at *13–14.

10x timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

II. STANDARD OF REVIEW

"We review the Board's legal conclusions de novo and its fact findings for substantial evidence." *Game & Tech. Co. v. Wargaming Grp. Ltd.*, 942 F.3d 1343, 1348 (Fed. Cir. 2019). "Whether a claimed invention is unpatentable as obvious is a question of law that is reviewed de novo, based on underlying findings of fact reviewed for substantial evidence." *Redline Detection, LLC v. Star Envirotech, Inc.*, 811 F.3d 435, 449 (Fed. Cir. 2015). Whether a person of ordinary skill in the art would have been motivated to combine prior art references is a factual question that we review for substantial evidence. *Intel Corp. v. PACT XPP Schweiz AG*, 61 F.4th 1373, 1378 (Fed. Cir. 2023).

"Substantial evidence means such relevant evidence as a reasonable mind might accept as adequate to support a conclusion." *FanDuel, Inc. v. Interactive Games LLC*,

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[4] U.S. Patent App. Pub. No. 2007/0020640 (filed July 21, 2005; published Jan. 25, 2007), 25-1618 J.A. 3272–90 ("McCloskey II").

966 F.3d 1334, 1343 (Fed. Cir. 2020) (internal quotation marks and citation omitted). "The substantial evidence standard . . . involves examination of the record as a whole, taking into account evidence that both justifies and detracts from an agency's decision." *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1381 (Fed. Cir. 2019) (internal quotation marks and citation omitted).

III. DISCUSSION

10x raises four challenges to the Board's final written decisions. First, for the '013 patent IPR, 10x argues that the Board never made a finding that a person of ordinary skill in the art would have been motivated to combine Linnarsson and McCloskey to reduce amplification bias and to use ligation to attach the second tag sequence. No. 25-1618 Appellant's Br. 31–32. Second, for the '197 patent and '981 patent IPRs, 10x argues that the Board erred in finding that a person of ordinary skill in the art would have found that a reduction of amplification bias or a design choice provides a motivation to combine Linnarsson and McCloskey. *Id.* at 32–61; No. 25-1199 Appellant's Br. 30–57. Third, for the '981 patent IPR, 10x argues that the Board erred in determining that the combination of Linnarsson and McCloskey discloses the "correlate" limitations. No. 25-1199 Appellant's Br. 57–61. Fourth, for the '197 patent and '981 patent IPRs, 10x argues that the Board erred in finding that a person of ordinary skill in the art would have been motivated to combine Linnarsson and McCloskey using ligation as a "design choice" that increased "flexibility." *Id.* at 61–65; No. 25-1618 Appellant's Br. 61–66. We address each argument in turn.

A.

10x argues that, for the '013 patent IPR, the Board committed reversible error because it never made any finding regarding the motivation to combine Linnarsson and McCloskey to add a second tag sequence and only discussed

the motivation for modifying that combination to use ligation. No. 25-1618 Appellant's Br. 31–32. We disagree.

The Board did not err in addressing the motivation-to-combine challenges that 10x raised before it. Before the Board, 10x never raised the motivation-to-combine challenges that it is raising before us now. Instead, 10x focused its motivation-to-combine arguments before the Board on utilization of ligation to add a tag and the length of the second tag from McCloskey that would be applied to Linnarson. No. 25-1618 J.A. 13356–61, 13382. Accordingly, the Board did not err by addressing the specific challenges that 10x raised. *'013 Decision* at *16–18; *see Novartis AG v. Torrent Pharms. Ltd.*, 853 F.3d 1316, 1327–28 (Fed. Cir. 2017).

Additionally, 10x does not show reversible Board error in the motivation-to-combine discussion. "[T]o prevail[, 10x] must not only show the existence of error, but also show that the error was in fact harmful because it affected the decision below." *In re Watts*, 354 F.3d 1362, 1369–70 (Fed. Cir. 2004). In this case, the Board acknowledged Parse's proposed motivations to combine, engaged specifically with the arguments that 10x disputed, and ultimately agreed with Parse's motivations to combine. *'013 Decision* at *15–19. The Board's finding in the '013 patent IPR that there was a motivation to combine McCloskey and Linnarsson is also consistent with the outcome of its findings for the '981 patent and '197 patent IPRs, where the Board found that there was a motivation to combine McCloskey and Linnarsson based on similar rationales that Parse raised for the '013 patent IPR, and which we discuss below. *Id.*; *'981 Decision* at *14–17; *'197 Decision* at *15–20. *Compare* No. 25-1618 J.A. 11056–58 *with* No. 25-1618 J.A. 13050–52 (arguing the same amplification bias motivation-to-combine rationale in the '197 patent and '013 patent petitions). Accordingly, 10x does not show reversible Board error in the motivation-to-combine discussion.

B.

10x challenges the Board's findings that a person of ordinary skill in the art would have been motivated to combine McCloskey and Linnarsson. 25-1199 Appellant's Br. 30–57; 25-1618 Appellant's Br. 32–61. For the '981 and '197 patent IPRs, the Board found that there was a motivation to combine because doing so: (1) would have been an obvious design choice, *'981 Decision* at *14–15; *'197 Decision* at *16; and (2) would have solved the problem of amplification bias, disclosed in Linnarsson, *'981 Decision* at *15–17; *'197 Decision* at *16–20; No. 25-1199 J.A. 1121 p. 2 ll. 11–13. Amplification refers to "a process by which extra or multiple copies of a particular polynucleotide are formed," No. 25-1199 J.A. 1131 p. 12 ll. 17–18, and amplification bias can lead to a "source-uncertainty problem for DNA sequences." No. 25-1199 J.A. 1190. 10x argues that the combination would not reduce amplification bias because McCloskey does not have enough barcodes to uniquely tag substantially all messenger RNA ("mRNA") molecules of Linnarsson. No. 25-1199 Appellant's Br. 30–48; No. 25-1618 Appellant's Br. 32–53. Specifically, 10x argues that: (1) the Board improperly deviated from the petition by relying on barcodes longer than the seven-nucleotide barcodes discussed in McCloskey, No. 25-1199 Appellant's Br. 32–37, No. 25-1618 Appellant's Br. 34–40; (2) eliminating amplification bias requires tagging substantially all mRNA molecules in a given cell, No. 25-1199 Appellant's Br. 37–44, No. 25-1618 Appellant's Br. 40–48; and (3) the Board erred by relying on Parse's arguments regarding bacteria and yeast, No. 25-1199 Appellant's Br. 44–48, No. 25-1618 Appellant's Br. 49–53. As explained below, we disagree.

i.

Substantial evidence supports the Board's findings that McCloskey is not limited to seven-nucleotide barcodes. As an initial matter, 10x is incorrect in arguing that Parse

relied on seven-nucleotide barcodes. Parse's petitions do not explicitly limit the number of nucleotides for the barcode. No. 25-1199 J.A. 8067 (discussing "McCloskey's teachings" rather than specifying a nucleotide count); No. 25-1618 J.A. 11058 (same). Furthermore, McCloskey itself does not teach only seven-nucleotide barcodes—although McCloskey states that it "currently use[s] seven nucleotides for the barcode," No. 25-1199 J.A. 1193. McCloskey also teaches the relationship between barcode length and the number of different molecules and how to change the number of distinguishable barcodes: "[t]he number of distinguishable barcodes in a population of oligonucleotides used in a reaction is determined by the number of random bases, *n*. This enables one to distinguish among 4^n allele copies per reaction." *Id.*; *see also* No. 25-1199 J.A. 3676–78; No. 25-1618 J.A. 3694–96. Accordingly, substantial evidence supports the Board's findings that McCloskey is not limited to seven-nucleotide barcodes.

ii.

10x argues that the Board erred in not finding that the rationale of reducing amplification bias requires substantially all the mRNA molecules present in a cell to be tagged because: (1) the Board "failed to address Linnarsson's teaching of tagging substantially all mRNA molecules," No. 25-1199 Appellant's Br. 38–40; No. 25-1618 Appellant's Br. 41–44; and (2) the Board failed to explain "how tagging less than substantially all mRNA molecules in a cell would address amplification bias," No. 25-1199 Appellant's Br. 40–44; No. 25-1618 Appellant's Br. 44–48. We address each argument in turn.

First, the Board did not fail to address Linnarsson's teaching of tagging substantially all mRNA molecules. The Board addressed 10x's argument and considered whether Parse's proposed combination required tagging each poly-

nucleotide or merely each sample polynucleotide[5] to address amplification bias. *'981 Decision* at *16–17; *'197 Decision* at *18–19.

Second, substantial evidence supports the Board's findings that Parse's rationale of reducing amplification bias does not require all the mRNA molecules present in a cell to be tagged. 10x concedes that the claims do not require all the mRNA molecules present in a cell to be tagged. No. 25-1199 J.A. 8407 ("[T]he claims don't require 'tagging all the mRNA molecules[.]'" (internal citation omitted) (emphases omitted)); No. 25-1618 J.A. 11584 (same). Additionally, Parse's rationale of reducing amplification bias does not require tagging substantially all the mRNA molecules present in a cell. In its petitions, Parse explains that McCloskey addresses amplification bias "[b]y incorporating a second tag in an oligonucleotide that uniquely identifies each sample polynucleotide prior to amplification." No. 25-1199 J.A. 8066; No. 25-1618 J.A. 11057–58; *see also* No. 25-1199 J.A. 1190, 1195. Parse consistently refers to tagging each *sample* polynucleotide in its petitions, not *each, every,* or *all* polynucleotides. No. 25-1199 J.A. 8066 (referring to tagging "each sample polynucleotide"); No. 25-1618 J.A. 11057 (same). Furthermore, expert testimony that the method would associate a tag with substantially every *sample* mRNA molecule supports the amplification-bias rationale. No. 25-1199 J.A. 1096. Accordingly, substantial evidence supports the Board's finding that not all the polynucleotides present in a cell must be tagged to support the rationale of reducing amplification bias.

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[5] "[S]ample polynucleotides are the polynucleotides in a cell that are being sampled (i.e., the polynucleotides of interest)[.]" *'197 Decision* at *18 (internal citation omitted) (emphasis omitted).

iii.

Substantial evidence supports the Board's findings that Linnarsson is not limited to mammalian cells. As an initial matter, this argument is not new or improperly raised in the reply. Parse explains in its petitions that "Linnarsson explains that the sample of single cells can take various forms" and can be obtained "from a tissue of interest, or from a biopsy, blood sample, or cell culture." No. 25-1199 J.A. 8050–51 (quoting No. 25-1199 J.A. 1132 p. 13 ll. 11–12); No. 25-1618 J.A. 11044 (same). Linnarsson itself is also not limited to mammalian cells. No. 25-1199 J.A. 1132 p. 13 ll. 14–16 ("Furthermore, in general, cells from any population can be used in the methods, such as a population of prokaryotic or eukaryotic single celled organisms including bacteria or yeast."). Accordingly, substantial evidence supports the Board's finding that Linnarsson is not limited to mammalian cells. *'981 Decision* at *16 ("Linnarsson is not limited to mammalian cells. Nor is the Petition's reliance on Linnarsson limited to mammalian cells."); *'197 Decision* at *18 (same, additionally explaining that the Petition's reliance on Linnarsson is not limited to eukaryotic cells).

Because we conclude that the Board's findings of a motivation to combine McCloskey and Linnarsson to reduce amplification bias are supported by substantial evidence, we do not reach 10x's arguments regarding a "design choice" rationale for ground 1 of the '981 patent and '197 patent IPRs, No. 25-1199 Appellant's Br. 49–57; No. 25-1618 Appellant's Br. 53–61, as the Board found amplification bias to be an independent motivation to combine, *'981 Decision* at *14 (finding the amplification-bias-reduction and obvious-design-choice rationales "independently sufficient to support the proposed modification"); *'197 Decision* at *15 (same).

C.

10x argues that the Board erred in determining that the combination of Linnarsson and McCloskey discloses the "correlate" limitations of the '981 patent because McCloskey's batch-stamp tracks batches, not individual cells. No. 25-1199 Appellant's Br. 57–61. We disagree.

Substantial evidence supports the Board's determination that the prior art discloses the "correlate" limitations of the '981 patent. The petition relies on Linnarsson for teaching the cell-specific tag, not McCloskey. No. 25-1199 J.A. 8069–70 (discussing Linnarsson as disclosing the "first tag sequence"); No. 25-1199 J.A. 8070–71 (identifying the combination of Linnarsson and McCloskey as disclosing the "second tag sequence"); *see also '981 Decision* at *14. Moreover, the proposed modification is that "Linnarsson's native tag would be conceptually divided into two portions, wherein the first portion performs the function of McCloskey's 'batch-stamp,' used to track individual cells." *'981 Decision* at *13 (citing No. 25-1199 J.A. 1097) (cleaned up). Because Linnarsson's native tag tracks a polynucleotide to its source "cell," No. 25-1199 J.A. 1138 p. 19 ll. 9–10, 1170 fig. 3, Linnarsson alone satisfies the "first tag . . . correlate" limitation. *'981 Decision* at *14; '981 patent col. 30 l. 40. Accordingly, substantial evidence supports the Board's determination that the prior art discloses the "correlate" limitations.

D.

10x argues that the Board erred in finding that a person of ordinary skill in the art would be motivated to use ligation in the combination of Linnarsson and McCloskey for claim 5 of the '981 and '197 patents and claim 1 of the '013 patent as a "design choice" to increase "flexibility." No. 25-1199 Appellant's Br. 61–65; No. 25-1618 Appellant's Br. 61–66. We disagree.

Substantial evidence supports the Board's findings that a person of ordinary skill in the art would be motivated to introduce a "second tag" through ligation as an obvious design choice to add flexibility. The patents themselves explained that "[s]uch conventional techniques include . . . ligation." '981 patent col. 13 ll. 37–39. Additionally, expert testimony supports the statement that a person of ordinary skill in the art would be motivated to introduce a "second tag" to "address the problem of amplification bias, as expressly taught in McCloskey," and "[t]here are only two ways to include this second tag," one of which is ligation. No. 25-1199 J.A. 3689 (Dr. Cooper reply declaration); No. 25-1618 J.A. 3712 (same); No. 25-1618 J.A. 10374–75 (same); No. 25-1199 J.A. 1113–17 (Dr. Cooper declaration); No. 25-1618 J.A. 1112–16 (same); No. 25-1618 J.A. 10078–81 (same); *ACCO Brands Corp. v. Fellowes, Inc.*, 813 F.3d 1361, 1367 (Fed. Cir. 2016) (explaining that when a person of ordinary skill in the art is left with two design choices, "[e]ach of these two design choices is an obvious combination of prior-art elements"). Regarding flexibility, the petitions explain that the benefit of added flexibility is the option to add a second tag sequence later in the process, No. 25-1199 J.A. 8080; No. 25-1618 J.A. 11074; No. 25-1618 J.A. 13054, and expert testimony supports this rationale, No. 25-1199 J.A. 1116; No. 25-1618 J.A. 1115–16; No. 25-1618 J.A. 10081. Accordingly, substantial evidence supports the Board's findings that a person of ordinary skill in the art would be motivated to introduce a "second tag" through ligation as an obvious design choice to improve flexibility.

IV. CONCLUSION

We have considered 10x's remaining arguments and find them unpersuasive. We *affirm*.

AFFIRMED