

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

EMBODY, INC. and ZIMMER BIOMET HOLDINGS, INC.,
Petitioner.

v.

LIFENET HEALTH,
Patent Owner.

IPR2025-00248
Patent 10,137,223 B2

Before MICHAEL J. FITZPATRICK, ANNETTE R. REIMERS, and
CHRISTOPHER C. KENNEDY, *Administrative Patent Judges*.

FITZPATRICK, *Administrative Patent Judge*.

JUDGMENT
Final Written Decision
Determining All Challenged Claims Unpatentable
35 U.S.C. § 318(a)

I. INTRODUCTION

Embody, Inc. and Zimmer Biomet Holdings, Inc. (collectively, “Petitioner”) filed a Petition requesting *inter partes* review of claims 1–12 of U.S. Patent No. 10,137,223 B2 (Ex. 1001, “the ’223 patent”) pursuant to 35 U.S.C. § 311(a). Paper 2 (“Petition” or “Pet.”). Patent Owner, LifeNet Health, filed a Preliminary Response pursuant to 37 C.F.R. § 42.107(b). Paper 9 (“Prelim. Resp.”). We granted the Petition. Paper 14 (“Inst. Dec.”).

During the review, Patent Owner filed a Patent Owner Response (Paper 24 (“PO Resp.”)), Petitioner filed a Reply (Paper 27 (“Pet. Reply”)), and Patent Owner filed a Sur-Reply (Paper 30 (“PO Sur-Reply”)). Pursuant to our authorization, the parties filed papers identifying alleged improper Reply and Sur-Reply arguments and evidence, and responses to those papers. Papers 28, 29, 35, and 36. An oral hearing was held on May 6, 2026, and a transcript of the hearing is included in the record. Paper 42 (“Tr.”).

We have jurisdiction under 35 U.S.C. § 6, and this Final Written Decision, issued pursuant to 35 U.S.C. § 318(a), addresses issues and arguments raised during the review. For the reasons discussed below, we determine that Petitioner has proven, by a preponderance of the evidence, that claims 1–12 of the ’223 patent are unpatentable.

A. Real Parties in Interest

Petitioner identifies Embody, Inc. as the real party in interest. Pet. 3. Petitioner further identifies Zimmer Biomet Holdings, Inc. (“ZBH”) as a second real party interest “[o]ut o[f] an abundance of caution.” *Id.* Patent Owner identifies itself as the sole real party in interest. Paper 3, 1.

B. Related Matters

The parties identify *LifeNet Health v. Zimmer Biomet Holdings, Inc.*, Case No. 2:23-cv-00479 (E.D. Va.) as a related matter. Pet. 3; Paper 3, 1. Petitioner also filed a petition for *inter partes* review for related U.S. Patent No. 11,318,227 B2 in IPR2025-00249.

C. The '223 Patent

The '223 patent is titled “ALIGNED FIBER AND METHOD OF USE THEREOF.” Ex. 1001, code (54). The '223 patent issued from Application No. 14/776,106, which was filed as a Patent Cooperation Treaty (PCT) application on March 13, 2014. *Id.* at codes (21), (22). The '223 patent claims priority to Provisional Application No. 61/785,031, filed on March 14, 2013. *Id.* at code (60).

The '223 patent discloses a “scaffold comprising an aligned fiber” used for tissue engineering. *Id.* at 1:10–23. It describes the use of an electrospinning apparatus to create fibers as small as one nanometer that are aligned in one principal direction, rather than being randomly oriented. *Id.* at 2:17–19. This electrospinning apparatus includes one or more spinnerets that are used to extrude a polymer or oligomer solution to form fibers. *Id.* at 2:60–64. As a result of the electrospinning, the fibers may be aligned at a particular angle. *Id.* at 4:46–60.

The '223 patent further describes the use of fast Fourier transform (FFT) analysis to measure the degree of alignment of the electrospun fibers. *Id.* at 13:3–26. Specifically, the '223 patent indicates that the FFT analysis may be performed using the methods described in Chantal Ayres *et al.*, “*Measuring fiber alignment in electrospun scaffolds: a user’s guide to the 2D fast Fourier transform approach*” 19 J. BIOMATERIALS SCI., POLYMER

EDN 603–621 (2008) (“Ayres 2008”; Ex. 1010), which is incorporated by reference into the ’223 patent.¹ Ex. 1001, 13:16–24. The ’223 patent explains that an FFT analysis of the aligned fibers may have “adjacent major peaks with about 180° apart from each other.” *Id.* at 13:4–6. The ’223 patent further states that “[t]he ‘major peaks’ herein refer to peaks higher than the average of the peaks in the result.” *Id.* at 13:6–7.

Figure 8A of the ’223 patent is reproduced below.

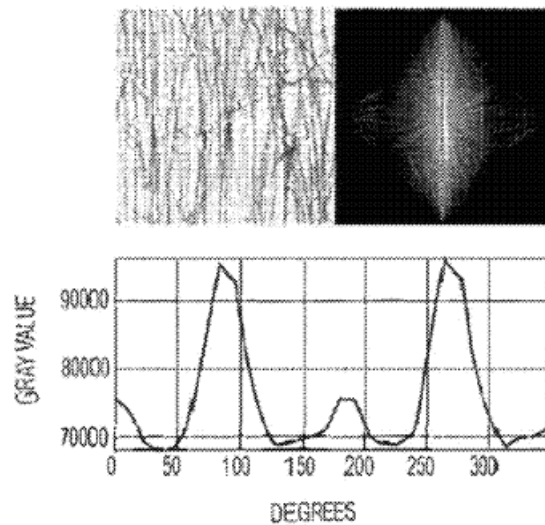


FIG. 8A

Ex. 1001, Fig. 8A. Figure 8A, reproduced above, includes three images and “depicts exemplary FFT analysis results [] of the [electrospun] fibers described” in the patent. *Id.* at 1:56–57; Ex. 2015 ¶51 (“The ’223 patent’s Figure 8A shows a FFT analysis result of aligned fibers.”)². The top left image above shows the electrospun fibers using a scanning electron microscope (SEM). Ex. 1001, 21:11–31. The top right image above shows

¹ Both parties agree Ayres 2008 is incorporated by reference into the ’223 patent. Pet. 26; PO Sur-Reply 4.

² Exhibit 2015 is a declaration by Patent Owner’s witness, Antonio G. Mikos, Ph.D.

the Fourier spectrum of the SEM image created using the “ImageJ64 FFT tool” reflecting a known pattern for aligned fibers. *Id.* at 21:27–31. The graph below those two images is a 2-dimensional FFT plot of the Fourier spectrum, showing major peaks at about 90° and 270° (i.e., about 180° apart) and smaller peaks at about 0° and 180°.

Figure 8B is reproduced below.

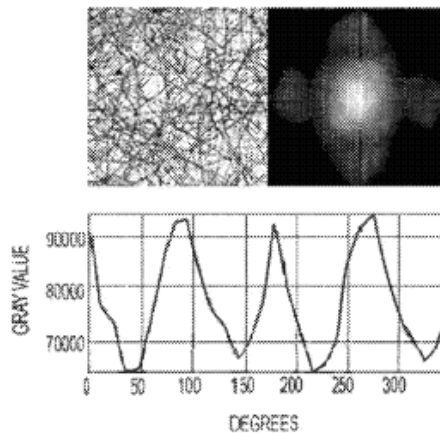


FIG. 8B

Ex. 1001, Fig. 8B. Figure 8B, reproduced above, includes three images and “depicts exemplary FFT analysis results [] of . . . a control sample” of randomly oriented fibers. *Id.* at 1:56–57; *see also* Ex. 2015 ¶51 (“Figure 8B as shown [sic] a control sample, e.g., with random fibers.”). Here, the 2-dimensional FFT plot (bottom image) of the Fourier spectrum (upper right image) shows at least three large but not uniform peaks at about 90°, 180°, and 270°, with the peak at about 180° being the shortest.³

³ Figure 8B may also show a fourth large peak at about 0°, but it is difficult to discern precisely where and even if the plot peaks at about 0°.

The '223 patent indicates that a variety of natural or synthetic materials may be used alone or blended to form aligned fibers according to the electrospinning techniques described therein. *Id.* at 7:10–30.

D. The Challenged Claims

Petitioner challenges claims 1–12 of the '223 patent. Claim 1 is the sole independent claim and recites the following:

1. A scaffold comprising one or more electrospun fibers comprising collagen, wherein a fast Fourier transform (FFT) analysis result of the fibers have [sic] adjacent major peaks with about 180° apart from each other.

Ex. 1001, 23:6–9.

E. The Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

Claim(s) Challenged	35 U.S.C. §⁴	Reference(s)/Basis
1–12	102	Huang2
4	103	Huang2, Kumbar
1–12	102	Lee
1–12	103	Lee

II. ANALYSIS

A. Level of Ordinary Skill in the Art

Petitioner proposes that a person of ordinary skill in the art (“POSITA”) “would be a Ph.D. student with a minimum of two years of

⁴ The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, which was enacted September 16, 2011, amended 35 U.S.C. §§ 102 and 103. AIA § 3(b)–(c). Those amendments became effective eighteen months later on March 16, 2013. *Id.* at § 3(n). Because the '223 patent claims priority to a provisional application filed before the effective date of the applicable AIA amendments (March 16, 2013), we refer to the pre-AIA versions of §§ 102 and 103 throughout this Decision.

experience in their faculty advisor’s laboratory” and would have an understanding of “electrospinning fibers, including for tissue engineering, tissue engineering techniques, and using/performing FFT analysis.” Pet. 18–19 (citing Ex. 1003 § II.C⁵). Patent Owner does not dispute Petitioner’s proposal but specifies the set of disciplines within which the Ph.D. would have been earned, namely “bioengineering, chemical engineering, mechanical engineering, or a related engineering discipline.” PO Resp. 5–6.

We adopt and apply Petitioner’s proposal as clarified by Patent Owner regarding the Ph.D. discipline.

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

Although we did not construe expressly any claim term in our institution decision based on the arguments presented at the time, the parties now dispute the meaning of “major peaks” as that term appears in the challenged claims. In particular, Patent Owner argues that the ’223 patent provides an express and exclusive definition of “major peaks,” namely:

⁵ Exhibit 1003 is a declaration by David G. Simpson, Ph.D., filed with the Petition.

“peaks higher than the average of the peaks in the result.” PO Resp. 6 (citing Ex. 1001, 13:6–7). Under this construction, Patent Owner argues that an FFT result cannot have major peaks unless it also has minor peaks. *See* PO Sur-Reply 7 (“To be clear: the claimed FFT result must have smaller/minor peaks; this is definitionally required to obtain an average height that is exceeded by ‘major peaks.’”).

Petitioner, on the other hand, disputes this lexicography-based construction in view of other evidence, both intrinsic and extrinsic. Pet. Reply 3–12. Given its importance to the overall patentability determination, it is necessary to resolve the parties’ claim construction dispute.

A patentee “may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history.” *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) (citing *Hoechst Celanese Corp. v. BP Chemicals Ltd.*, 78 F.3d 1575, 1578 (Fed. Cir. 1996)); *see Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc) (“[A]ny special definition given to a word must be clearly defined in the specification.”), *aff’d*, 517 U.S. 370 (1996); *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002). “[T]he intrinsic evidence must ‘clearly set forth’ or ‘clearly redefine’ a claim term so as to put one reasonably skilled in the art on notice that the patentee intended to so redefine the claim term.” *Bell Atlantic Network Services, Inc. v. Covad Communications Group, Inc.*, 262 F.3d 1258, 1268 (Fed. Cir. 2001).

Among the criteria to consider in whether the patentee acted as a lexicographer to define a claim term include (a) whether the patent specification included the statement in question under a section for

“definitions,” (b) whether the term to be defined is set off in quotation marks, (c) whether the sentence uses the term “refer to,” which generally “conveys an intent for [that sentence] to be definitional,” and (d) whether there are other non-limiting terms (e.g., “for example,” or “include”) that contradict a definitional intent. *Alnylam Pharms., Inc. v. Moderna, Inc.*, 138 F.4th 1326, 1333 (Fed. Cir. 2025) (alteration in original).

At the outset, we agree with Patent Owner that the Specification purports to define “major peaks” in the following sentence: “The ‘major peaks’ herein refer to peaks higher than the average of the peaks in the result.” Ex. 1001, 13:6–7. We determine that this language satisfies at least two of the criteria set forth in *Alnylam*. Specifically, the sentence at issue sets out “major peaks” in quotation marks, and then uses the term “refers to” to explain what qualifies as major peaks. That is not the end of the inquiry, however, as we find there is still some ambiguity as to whether the patentee intended to define “major peaks” so as to require so-called “minor peaks” in the claimed invention. *See Bell Atlantic*, 262 F.3d at 1268 (“[T]he intrinsic evidence must ‘clearly set forth’ or ‘clearly redefine’ a claim term so as to put one reasonably skilled in the art on notice that the patentee intended to so redefine the claim term.”).

Importantly, the Specification does not treat the existence of minor peaks as prerequisites for the existence of major peaks. Indeed, the Specification does not discuss “minor peaks” at all. *See generally* Ex. 1001. Likewise, none of the claims of the ’223 patent, whether challenged or unchallenged, recites “minor peaks” or any additional peaks beyond the disputed “major peaks.” *Id.* at 23:6–24:41. Nor does the Specification include an example of FFT analysis results in which the average of the peaks

therein is calculated and those higher than the average are identified as major peaks.⁶

Rather, it appears, based on both the Specification as well as extrinsic evidence, that the named inventors of the '223 patent assumed that an FFT analysis would *always* contain additional peaks that are not major peaks because it was thought impossible to manufacture a scaffold of perfectly aligned fibers. For example, at oral argument, counsel for Patent Owner stated the following in response to questioning from the Board:

JUDGE KENNEDY: Counsel, this is Judge Kennedy. I have a quick question for you. So given your apparent position that the claim requires there to be minor peaks, is it also your position that the claim excludes a perfectly aligned scaffold?

MS. WIEKER: So the claim is directed to a real-world manufactured scaffold. For example, we've got this slide up here, and I'll direct you to Slide 9, as you see in Figure 8A [of the '223 patent]. The claim is directed to a real-world scaffold that has a principal axis of alignment that's represented by major peaks and additional axes of alignment reflected by minor peaks. And you can see that in the SEM image that's in the upper left of the slide.

So for example, the Ayres spaghetti strand example, that is perfectly aligned fibers, but it does not produce this FFT result because it does not have the major and minor peaks that are definitionally required.

⁶ Indeed, as discussed *infra*, if such a calculation were applied to the FFT analysis result illustrated in Figure 8B, it would indicate that Figure 8B includes two major peaks at about 90° and 270° (i.e., about 180° apart), yet the '223 patent states that Figure 8B relates to random fibers. See Ex. 1001, 1:56–57 (stating Figure 8B shows “exemplary FFT analysis results” of “a control sample” of randomly oriented fibers); Ex. 2015 ¶51 (“Figure 8B as shown [sic] a control sample, e.g., with random fibers.”).

JUDGE KENNEDY: So your claim, whether you want to call it a real-world scaffold or a slightly misaligned scaffold, your claim would require there to be at least some misalignment?

MS. WIEKER: Some minor peaks, yes. And as we just discussed, the peaks reflect fiber alignment, so it's going to be an additional or secondary axis of alignment.

Tr. 45:10–46:6; *see also* PO Sur-Reply 7 (Patent Owner's proposal for requiring minor peaks "reflects real-world scaffolds where 'high frequency signals' that 'reflect fiber alignment' are plotted as 'prominent or "major" peaks,' and where 'fibers that present additional orientations' are plotted as 'smaller or minor peaks.'"). This is consistent with Figure 8A of the '223 patent, which "depicts exemplary FFT analysis results [] of the [electrospun] fibers described" in the patent. Ex. 1001, 1:56–57. Figure 8A is reproduced below.

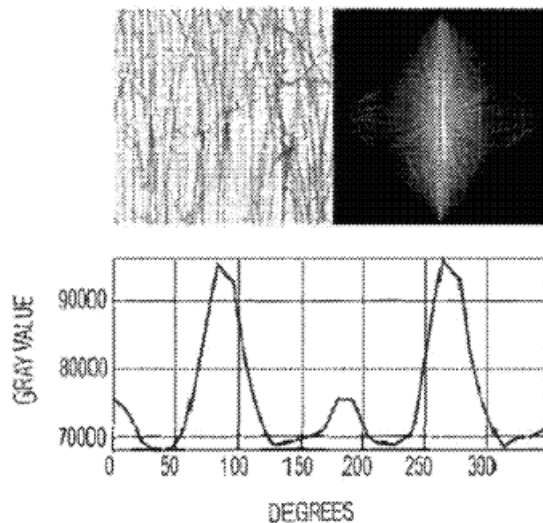


FIG. 8A

Ex. 1001, Fig. 8A. Figure 8A, reproduced above, includes three images. The top left image shows a SEM image of electrospun fibers. *Id.* at 21:11–31. As can be seen in the image, the fibers are predominantly aligned in a vertical orientation but several fibers are not so aligned. Consistent with

some misalignment, the 2-dimensional FFT plot (bottom image) of the Fourier spectrum (top right) includes, not only major peaks at about 90° and 270°, but also smaller peaks at about 0° and 180°.

During continued questioning from the Board, counsel for Patent Owner implicitly argued that the challenged claims require some misalignment because they require minor peaks.

JUDGE KENNEDY: Given your specification[']s focus on alignment, is there any statement in the specification that makes clear that some misalignment is actually required, or you just have to read that into the definition of major peaks?

MS. WIEKER: So here, the patentee certainly could have claimed aligned fibers had they intended that to cover their invention, but what they did was elect to provide a specific definition that requires an FFT result with major peaks and define those major peaks as higher than an average. And there's no way to understand that clear definition except from its requirement that there be minor peaks that are exceeded.

Tr. 46:7–17.

We are not satisfied by the purported distinction Patent Owner attempts to delineate. As discussed above, the '223 patent never discusses “minor peaks,” let alone as a requirement of the claimed invention.

The term “major peaks” must be read in light of the entire Specification. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (“the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification”). Here, the Specification repeatedly emphasizes that the disclosed invention relates to aligned fibers. *See, e.g.*, Ex. 1001, code (54) (“ALIGNED FIBER AND METHOD OF USE THEREOF”), code (57) (“A scaffold comprising an aligned fiber.”), 1:6–7 (“The invention relates to an

aligned fiber and method of use thereof.”), 1:11–12 (“The invention relates to a scaffold comprising an aligned fiber.”). The Specification does not state, or even suggest, that the claimed invention is limited to a scaffold of *merely predominantly* aligned fibers. In other words, the Specification does not state that the claimed invention is limited to scaffolds that have *some* misalignment and/or secondary alignment.

We acknowledge that the Specification also states that “[t]he invention further relates to a scaffold comprising one or more electrospun fibers wherein a fast Fourier transform (FFT) analysis result of the fibers have adjacent major peaks with about 180[°] apart from each other.” *Id.* at code (57); *see also id.* at 1:13–16 (“In some embodiments, wherein [sic] a fast Fourier transform (FFT) analysis result of the fibers have adjacent major peaks with about 180° apart from each other.”). However, the Specification explains that FFT is a tool for measuring alignment of the fibers. *Id.* at 13:16–17 (“Alignment of the fibers in the scaffold may be measured by a fast Fourier transform (FFT) analysis.”). This is not to suggest that we ignore the claim language reciting “wherein a fast Fourier transform (FFT) analysis result of the fibers have [sic] adjacent major peaks with about 180° apart from each other.” We give that language full weight, but we will not interpret the term “major peaks” so as to rewrite the language as requiring both minor peaks and major peaks in the FFT analysis result.

Although the Specification draws a clear distinction between random fibers (Fig. 8B) and aligned fibers (Fig. 8A), the Specification does *not* draw any distinction *between mostly aligned fibers and uniformly aligned fibers*. We cannot uncritically accept Patent Owner’s purported definition of “major peaks” so as to construe the claims to require so-called “minor peaks” that the claims do not affirmatively recite and which the Specification does not

describe. *See Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248 (Fed. Cir. 1998) (“[A] claim must be read in view of the specification of which it is a part.”). This is especially true given the ’223 patent’s focus on creating “a scaffold comprising an aligned fiber,” whereas so-called “minor peaks” would be an indication of non-uniform alignment. Tr. 45:10–46:6; cf. *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1383 (Fed. Cir. 2009) (Lourie, J., dissenting) (“This case illustrates the unusual situation in which a purported definition of a claim term in the written description is totally negated by the remainder of the text of the patent. Martek’s attempt at lexicography does not conform to the way in which it otherwise describes its invention.”).⁷

Furthermore, adopting Patent Owner’s purported definition of “major peaks” would be inconsistent with the Specification’s description of Figure 8B as “depict[ing] exemplary FFT analysis results [] of . . . a control sample” of randomly oriented fibers. Ex. 1001, 1:56–57; *see also* Ex. 2015 ¶51 (“Figure 8B as shown [sic] a control sample, e.g., with random fibers.”); PO Resp. 5 (stating that Figure 8B shows “non-aligned fibers”). Figure 8B again is reproduced below.

⁷ As we note above, the cited language in *Martek Biosciences* comes from a dissenting opinion. To be clear, the majority opinion in that case does not support Patent Owner’s position here. In *Martek Biosciences*, the majority enforced lexicography that resulted in a broader, not narrower, claim scope than that being proposed by the adversary and, importantly, it did not require the addition of an unstated limitation. *See* 579 F.3d at 1382 (“The proper construction for the claim term ‘animal’ is the one explicitly provided by the patentee [in the patent]: ‘any organism belonging to the kingdom Animalia,’ which includes humans.”). Here, Patent Owner asks us to narrow the claim scope by incorporating an unstated limitation, the presence of minor peaks.

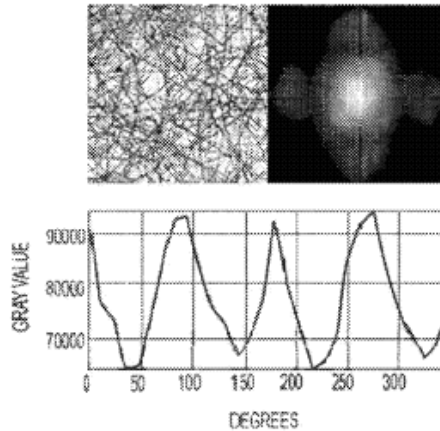


FIG. 8B

Ex. 1001, Fig. 8B. Figure 8B, reproduced above, includes three images. As pointed out by Petitioner, under Patent Owner’s purported definition of “major peaks,” the FFT analysis depicted in the bottom image of Figure 8B has “adjacent major peaks with about 180° apart from each other” (i.e., at about 90° and 270°) as recited in claim 1. Pet. Reply 8–9; Ex. 1219 ¶¶8–19.⁸ This is so because those two peaks are higher than the average of the total of the three peaks that are shown (or four peaks if including one at 0°). But the Specification clearly disavows Figure 8B from the scope of the claims. Ex. 1001, 1:56–57.

In its Sur-Reply, Patent Owner attempts to obviate this potential conflict. In that regard, Patent Owner first argues that “Figure 8B depicts a ‘control’ sample of random fibers, *where no peaks exceed the average height (within conventional bounds of experimental error).*” PO Sur-Reply 4 (emphasis added). However, no citation is provided to support the italicized portion of the argument, which thus constitutes unpersuasive

⁸ Exhibit 1219 is a subsequent declaration by Dr. Simpson that Petitioner filed with its Reply.

attorney argument. *See, e.g., Icon Health & Fitness, Inc. v. Strava, Inc.*, 849 F.3d 1034, 1043 (Fed. Cir. 2017) (“Attorney argument is not evidence.”).

Next, Patent Owner argues that “Ayres-2008, incorporated by reference [into the ’223 patent], likewise explains, ‘peaks of *nearly uniform height*’—like Figure 8B—indicate a random scaffold.” PO Sur-Reply 4 (citing Ex. 1010, 609; Ex. 2017, 88:7–15). It is true that Ayres 2008 is incorporated by reference into the ’223 patent. Ex. 1001, 13:16–23. It is also true that Ayres 2008 states: “Peaks of nearly uniform height are a hallmark of a scaffold composed of random elements.” Ex. 1010, 609. However, this teaching by Ayres 2008 does not obviate the conflict in Patent Owner’s position. To the contrary, it highlights the conflict, as it is further evidence that Figure 8B shows results obtained from “a scaffold composed of random elements.” *Id.* Yet, if the purported definition of “major peaks” were adopted and applied literally, Figure 8B would come within the scope of claim 1, which would be a clearly erroneous and nonsensical result.⁹ Thus, Ayres 2008 does not support Patent Owner’s construction.¹⁰

As discussed above, we agree with Patent Owner that the sentence it cites from the Specification of the ’223 patent bears sufficient hallmarks of lexicography. However, the Specification nonetheless lacks any indication that so-called “minor peaks” are a necessary component of the claimed invention. “Although it is firmly settled that an applicant may act as a

⁹ Figure 8B does not contain “major peaks” despite clearly depicting two “peaks higher than the average of the [three or possibly four] peaks in the result” because none of the peaks is a reflection of fiber alignment.

¹⁰ After presenting claim construction arguments based on Ayres 2008, Patent Owner confusingly states: “Finally, whether Ayres-2008 supports [Patent Owner’s] construction *is irrelevant*.” PO Sur-Reply 5 (emphasis added).

lexicographer in the specification, . . . the specification cannot support a definition that is contrary to the ordinary meaning of a claim term unless it communicates a deliberate and clear preference for this alternative definition.” *Kumar v. Ovonic Battery Co.*, 351 F.3d 1364, 1368 (Fed. Cir. 2003). There is no indication that the patentee sought to require “minor peaks” within the scope of the claimed invention. Nor are we persuaded that a person of ordinary skill in the art would readily understand the scope of the term “major peaks” to require non-major peaks.

We interpret the Specification’s statement that “‘major peaks’ herein refer to peaks higher than the average of the peaks in the result” (Ex. 1001, 13:6–7) to be teaching a person of ordinary skill in the art how to identify or discern “major peaks,” which indicate a principal axis of alignment, from any non-major peaks, which would be caused by something else.

We conclude that a person of ordinary skill in the art would consider “major peaks” as used in the ’223 patent as referring to peaks that reflect the sole axis or primary axis of fiber alignment. *See, e.g., id.* at code (54) (“ALIGNED FIBER AND METHOD OF USE THEREOF”), code (57) (“A scaffold comprising an aligned fiber.”), 1:6–7 (“The invention relates to an aligned fiber and method of use thereof.”), 1:11–12 (“The invention relates to a scaffold comprising an aligned fiber.”), 13:16–17 (“Alignment of the fibers in the scaffold may be measured by a fast Fourier transform (FFT) analysis.”). This would certainly include peaks materially higher than the average of the peaks in the result, but it would not be limited to situations involving peaks of different heights or require so-called minor peaks. Based on the totality of the evidence before us, we do not construe the claims to require non-major peaks.

C. The Prior Art

1. Huang2 (Ex. 1005)

Chengyang Huang et al., *The involvement of integrin $\beta 1$ signaling in the migration and myofibroblastic differentiation of skin fibroblasts on anisotropic collagen-containing nanofibers*, 33 *Biomaterials* 1791–1800 (Feb. 2012) (“Huang2”) is a journal article that was first published online on December 2, 2011. Ex. 1005, 1791.¹¹ Huang2 qualifies as prior art under pre-AIA 35 U.S.C. § 102(b). Pet. 21. Patent Owner does not dispute that Huang2 is available as prior art.

Huang2 studies collagen fibers used for tissue-engineered skin grafts. Ex. 1005, 1791. In particular, Huang2 compares aligned (anisotropic) fibers to non-aligned (isotropic) fibers¹² with regard to their effect on the attachment and growths of normal human dermal fibroblasts (“NHDFs”). *Id.* To mimic the skin’s native extracellular matrix (“ECM”), Huang2 discusses creating scaffolds of electrospun collagen fibers. *Id.* Huang2 teaches that, when doing so, “either crosslinking or blending with other materials is necessary to obtain a stable scaffold.” *Id.* Huang2 states that, for the scaffolds that its researchers fabricated, blending with

¹¹ A different reference by Huang, identified as “Huang1” (Ex. 1008) in the Petition, was considered by the Examiner during prosecution. *See* Pet. 15–17 (citing Ex. 1002, 210–211).

¹² Isotropic fibers are randomly oriented, and anisotropic fibers are aligned. *See* Ex. 1005, 1792 (“To address this hypothesis together with the attempt to mechanistically understand fiber alignment-induced cell migration, normal human dermal fibroblasts (NHDFs) were seeded on collagen-containing PCL nanofibrous matrices with either isotropic nanofiber arrangement (*i.e.*, randomly collected nanofibers with no alignment, abbreviated as ‘*Iso*’) or anisotropic nanofiber arrangement (*i.e.*, collected nanofibers with alignment, abbreviated as ‘*Aniso*’).”).

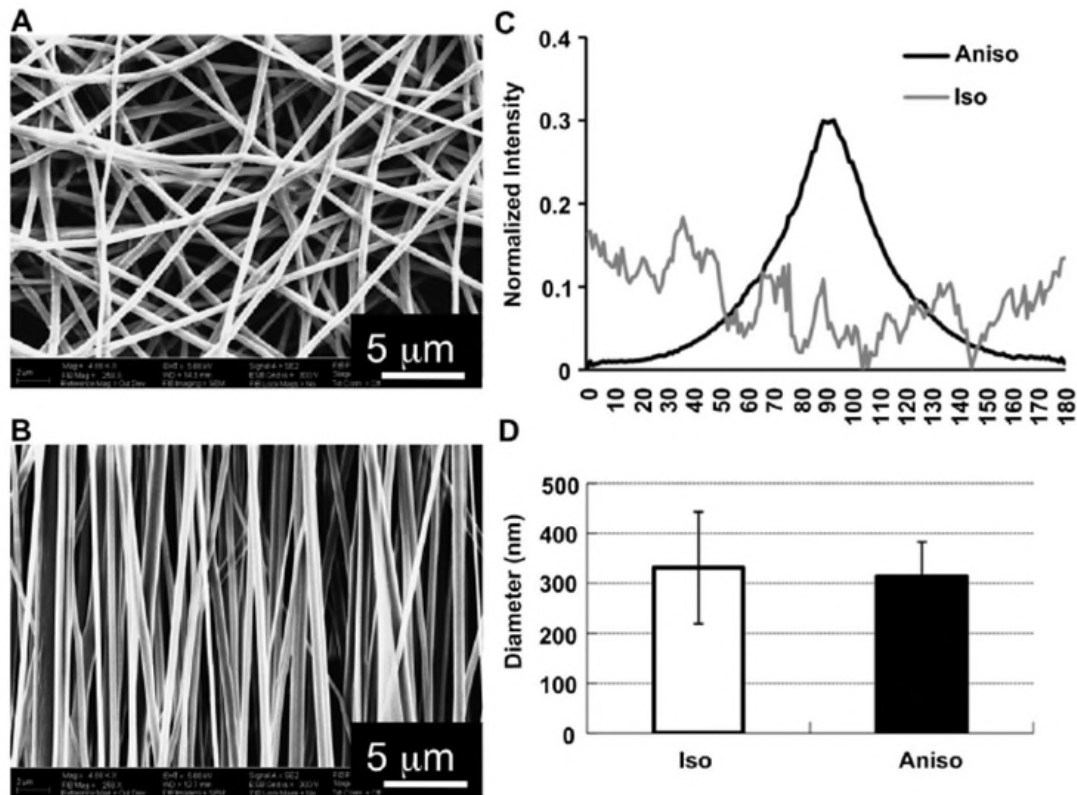
polycaprolactone (PCL) was used. *See id.* at 1792 (“Nanofibrous matrices of PCL and Collagen at a weight ratio of 3:1 were fabricated using electrospinning as previously described.”).

Huang² characterizes both isotropic and anisotropic PCL/collagen blends in several ways, including by SEM and FFT analysis. With regard to FFT analysis, Huang 2 discloses:

The orientation of electrospun nanofibers was determined by using the ImageJ program (NIH) along with the Oval Profile Plot plugin [22¹³]. Briefly, representative SEM images of the electrospun fibers were cropped into a square covering as much of the image as possible (the images used were 905 x 905 pixels in size). These cropped images were then processed with a fast Fourier transform (FFT) and then a circular section of the image was made maximizing the amount selected (edges of the circle were tangent with the edges of the image). This selection then underwent a radial summation using the Oval Profile Plot plugin with 360 points such that the degree interval was 1°. The raw data were normalized to 0 and data from all sets were rescaled to an arbitrary range between 0 and 0.3. The final results were presented by plotting this arbitrary scale *versus* degrees, where the height of the peaks represents a greater degree of alignment at a given angle.

Ex. 1005, 1792. The results are shown in Figure 1, reproduced below:

¹³ Reference [22] in Huang² refers to Chantal Ayres et al., “*Modulation of anisotropy in electrospun tissue-engineering scaffolds: analysis of fiber alignment by the fast Fourier transform*” 27(32) BIOMATERIALS 5524–34 (2006) (“Ayres 2006,” Ex. 1013). *See* Ex. 1005, 1800. Although not relied upon to teach any particular claim limitations, Ayres 2006 and Ayres 2008 are discussed below given their relevance to Petitioner’s patentability challenges.



Ex. 1005, Fig. 1. Figure 1A (top left) shows a SEM image of an isotropic (random fibers) sample of a PCL/collagen nanofibrous matrix, whereas Figure 1B (bottom left) shows a SEM image of an anisotropic (aligned fibers) sample. *Id.* at 1793. Figure 1C (top right) shows the normalized intensity plots against the angle of acquisition for the isotropic and anisotropic samples obtained using FFT analysis. *Id.* Figure 1D (bottom right) shows the measured average fiber diameter of both matrices. *Id.*

Huang2's results showed that fibroblast-to-myofibroblast differentiation, important to the reconstruction of connective tissue during wound healing, was enhanced in the anisotropic PCL/collagen nanofibers due to the impact of the alignment on the integrin $\beta 1$ signaling pathway. *Id.* at 1797–99.

2. *Kumbar (Ex. 1006)*

Kumbar et al., *Electrospun nanofiber scaffolds: engineering soft tissues*, Biomed. Mater. 3 (2008) (“Kumbar”) is a journal article published on August 8, 2008. Ex. 1006, 1. It qualifies as prior art under pre-AIA 35 U.S.C. § 102(b). Patent Owner does not dispute Kumbar’s availability as prior art. Huang² (discussed above) cites Kumbar in its discussion of the desirable properties of electrospun scaffolds. Ex. 1005, 1799 (reference [3]).

Kumbar describes research efforts in “designing nanofiber matrices as scaffolds in the regeneration of various soft tissues including skin, blood vessel, tendon/ligament, cardiac patch, nerve and skeletal muscle.” Ex. 1006, 1 (Abstract). Kumbar notes that “electrospun nanofiber matrices have gained a lot of attention, and are being explored as scaffolds in tissue engineering due to their properties that can modulate cellular behavior.” *Id.* Kumbar discloses the benefits of using collagen, explaining that “[c]ollagen nanofibers play a dominant role in maintaining the biological and structural integrity of various tissues and organs, including bone, skin, tendon, blood vessels and cartilage.” *Id.* at 7.

Kumbar also discloses desirable mechanical properties of scaffolds in tissue engineering. According to Kumbar, these properties are important “to provide cells with the necessary chemical cues and a more *in vivo* like environment” for use “in the regeneration of various soft tissues including skin[.]” *Id.* at 1 (Abstr.). Kumbar describes that “[f]iber alignment in nanofiber matrices significantly improves the mechanical properties.” *Id.* at 6. Kumbar further explains that “[n]anofiber matrices as tissue engineering scaffolds need to have interconnected highly porous structures to facilitate cellular migration and transport of nutrients, and metabolic wastes to allow the formation of new tissue.” *Id.* With respect to “[e]lectrospun nanofiber

skin grafts,” Kumbar notes that “[c]ross linking collagen nanofibers resulted in decrease of porosity from 89% to 71%.” *Id.* at 7.

3. *Lee (Ex. 1011)*

US 2010/0331980 A1, published Dec. 1, 2011 (“Lee”) was published on December 30, 2010. Ex. 1011, code (43). It qualifies as prior art under Pre-AIA 35 U.S.C. § 102(b). Patent Owner does not dispute Lee’s availability as prior art.

Lee is generally directed to an aligned scaffolding system for skeletal muscle regeneration. *Id.*, at code (54). Lee teaches that the reconstruction of skeletal muscle tissue lost, for example, due to a traumatic injury is difficult because of “the lack of available functional muscle tissue substitutes.” *Id.* at ¶3. To solve this problem, Lee describes engineered muscle tissue, including “a biodegradable scaffold comprising a plurality of fibers oriented along a longitudinal axis of the fibers” and “methods of forming a biodegradable scaffold, including the steps of: electrospinning a solution comprising a biodegradable scaffold material onto a grounded mandrel to form a plurality of fibers oriented along a longitudinal axis; and crosslinking said fibers to form the scaffold.” *Id.* ¶¶5–6. Lee explains that its “[s]caffold” refers to an array of natural or synthetic matrix molecules to which cells or fibers can attach,” which it further explains may include various components and molecules. *Id.* ¶44.

Lee describes using fibers for the scaffold that are natural, such as collagen, or synthetic, such as PCL, or blends of natural and synthetic fibers between 2:1 and 1:2 by weight. *Id.* ¶5. Lee also describes obtaining

electrospun nanofiber meshes¹⁴ “using a blend of PCL and collagen with a ratio of 1:1 in weight.” *Id.* ¶¶62–63. Lee explains that “PCL-collagen composite scaffolds according to some embodiments have preferable biomechanical properties, e.g., yield tensile strength, elasticity and compliance.” *Id.* ¶52. Lee teaches that when PCL and collagen are used together, there is “improved biocompatibility, mechanical properties, and processability,” and further explains that “in some embodiments the biomechanical properties of PCL-collagen scaffolds are similar to that of native tissue.” *Id.*

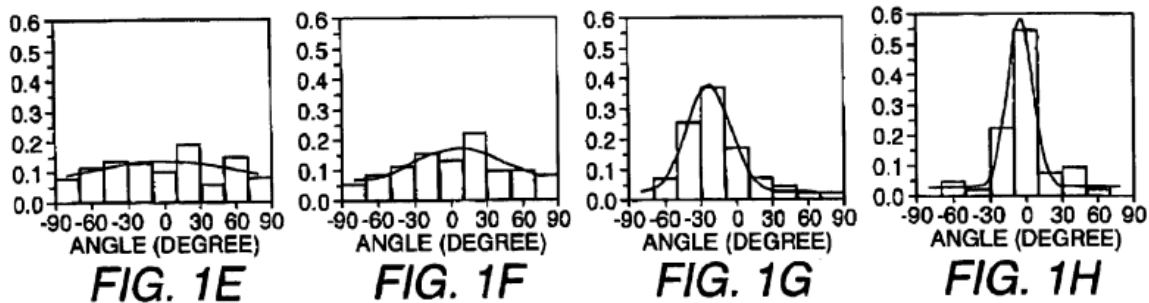
Further, Lee teaches fabricating “nanofiber meshes that are aligned in a unidirectional manner to facilitate myotube formation” in order to approximate skeletal muscle. *Id.* ¶90. Lee explains that previous studies demonstrated that “aligned nanofibrous structures can be obtained using a variety of collecting mandrel systems, including rotating drum.” *Id.* ¶91. Lee discovered that “[f]iber alignment had a profound effect on the mechanical properties of electrospun PCL/collagen nanofiber meshes,” including increased tensile strength for the aligned nanofiber meshes. *Id.* ¶81.

Lee explains that the aligned fibers aided in cell growth—“[t]he myotubes that formed on the oriented nanofiber meshes showed unidirectionally organized myotubes that are consistently aligned along the longitudinal axis of nanofibers, which is in contrast to the randomly oriented nanofiber meshes (FIGS. 5c, f).” *Id.* ¶84. While the “myotubes formed on

¹⁴ Lee uses the terms “scaffold,” “mesh,” and “matrix” interchangeably. *See* Ex. 1011 ¶45 (“A ‘biodegradable scaffold,’ ‘biodegradable mesh’ or ‘biodegradable matrix’ is a scaffold having materials capable of being degraded and/or absorbed in a subject’s body.”).

the randomly oriented nanofiber meshes . . . did not show a global cellular organization,” Lee states that the “myotubes on the aligned nanofiber meshes organized within close proximity to the direction of the nanofiber direction and formed globally aligned myotubes (FIG. 6d).” *Id.* ¶85.

Lee obtained SEM images and plotted histograms of fiber angles for fibers that were electrospun at different rates of rotation. *Id.* ¶11. Figures 1E–1H of Lee are reproduced below:



The figures above show normalized histograms of fiber angles obtained at different rates of rotation, ranging from “static” (Fig 1E on the left) to 2350 rpm (Fig. 1H on the right). *Id.* ¶11. As shown above, a distinct peak occurs in the histogram for fibers obtained at higher rates of rotation, which reflects the fiber orientation at that angle.

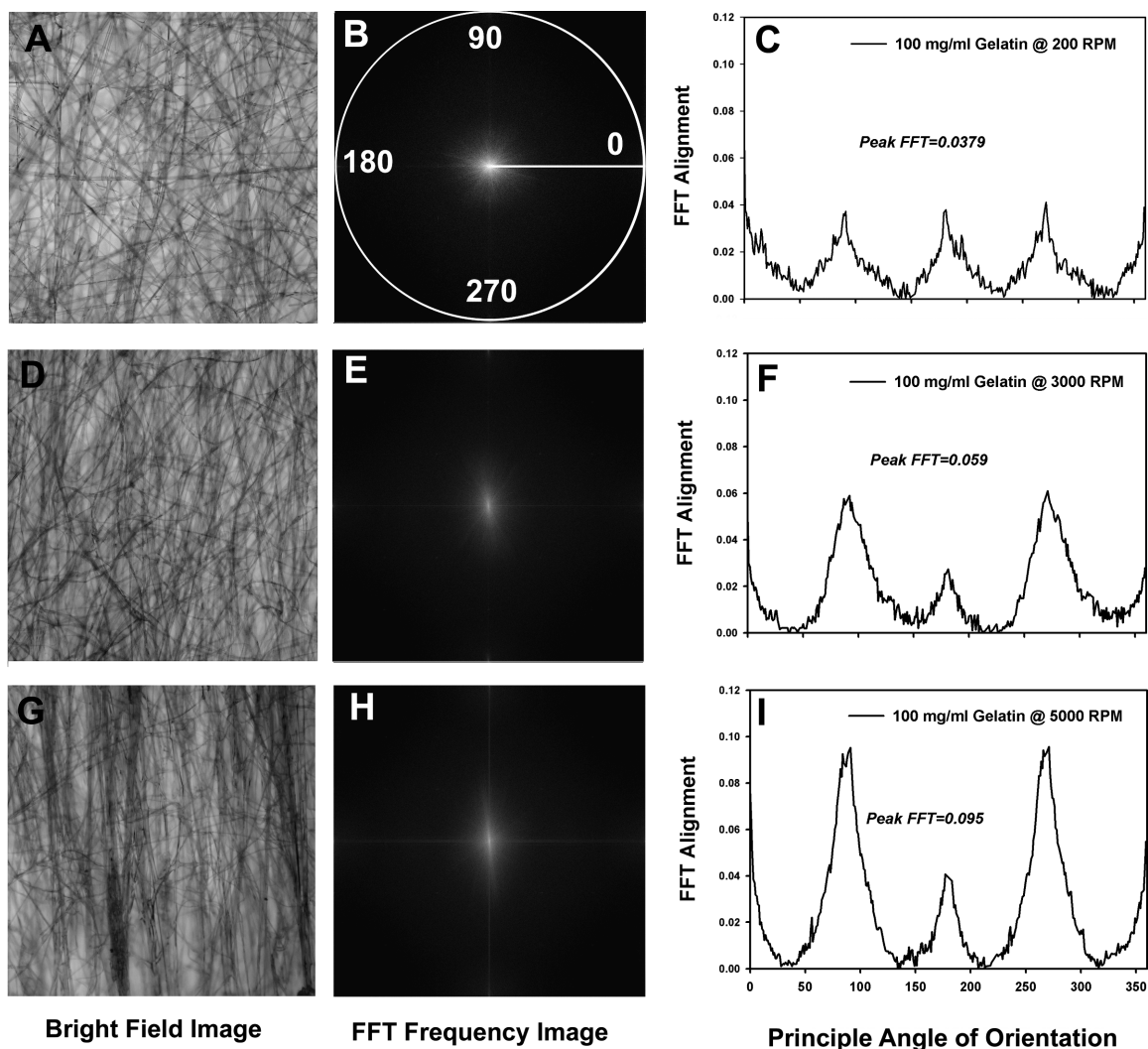
Lee concludes that the “[a]ligned nanofibers greatly influenced muscle cell organization and enhanced myotube formation,” and that “myotubes formed on the aligned nanofiber meshes were highly organized and were significantly longer than that of the myotubes on the randomly oriented meshes.” *Id.* ¶94. “These findings indicate that the electrospun PCL/collagen nanofiber meshes are able to guide and orient skeletal muscle cells into organized structures that mimic native tissues.” *Id.*

4. *Ayres 2008 (Ex. 1010)*

Ayres 2008 is an article published in JOURNAL OF BIOMATERIALS SCIENCE, POLYMER EDITION in 2008 and was later published online on April 2, 2012. Ex. 1010, 604. As noted above, Ayres 2008 was incorporated by reference into the '223 patent. Ex. 1001, 13:17–24. Petitioner's declarant, Dr. Simpson, is one of the named authors of Ayres 2008. Patent Owner does not dispute that Ayres 2008 qualifies as prior art.

Ayres 2008 describes a method of using two-dimensional fast Fourier transform (2D FFT) to measure fiber alignment in electrospun materials. Ex. 1010, 604. As explained in Ayres 2008, “[a] data image of an electrospun scaffold is composed of pixels that depict the spatial organization of the constituent fibers.” *Id.* at Abstr. “The 2D FFT function converts this spatial information into a mathematically defined frequency domain that maps the rate at which pixel intensities change across the original data image,” which thereby provides “quantitative information concerning the orientation of objects in a data image.” *Id.*; *see also id.* at 608. ImageJ software (obtained from the NIH) supported by an oval profile plug-in was used to conduct the 2D FFT analysis. *Id.* at 607.

Figure 1 of Ayres 2008 is reproduced below:



Ex. 1010, Fig. 1. Figures 1A, 1D, and 1G (left column) show brightfield images of representative electrospun scaffolds composed of fibers with varying degrees of alignment. Figures 1B, 1E, and 1H (middle column) show the ImageJ-generated “frequency plots,” while Figures 1C, 1F, and 1I on the right show the “2D FFT alignment plots” for the corresponding brightfield images.

As explained in Ayres 2008, “[w]hen an image of random fibers is processed by 2D FFT, the resulting frequency plot contains a cluster of white pixels that are concentrated in a symmetrical, circular pattern around the origin (Fig. 1B).” *Id.* at 609. On the other hand, the frequency plot for

an image of aligned fibers will contain pixels “concentrated along a specific axis” (Figs. 1E, 1H). *Id.* at 610. After rotating the frequency plot by 90°, the intensities of the pixels are summed along the radius for each angle of a circular projection (0–360°) placed on the image using the ImageJ software. *Id.* at 609. The summed pixel intensities are then plotted against the corresponding angle to produce the 2D FFT alignment plot. Although Figures 1C, 1F, and 1I show the alignment data for the full 360° projection, Ayres 2008 notes that “[t]ypically, the data from this analysis is reported for 0 to 180°” because “the frequency plot is symmetric so a complete summation from 0 to 360° is not technically necessary.” *Id.*

As depicted in Figure 1C, “[t]he 2D FFT alignment plot of a random matrix will exhibit 4 peaks that occur every 90°.” *Id.* By contrast, “[t]he 2D FFT alignment plots generated from sample scaffolds containing aligned elements exhibit asymmetrical peaks, two larger peaks at 90 and 270° and two smaller peaks at 0 and 360° (Fig. 1F and I).” *Id.* at 610. Ayres 2008 explains that “[t]he degree of alignment present in the original data image is reflected by the height and overall shape of the most prominent peaks present in the alignment plot.” *Id.*

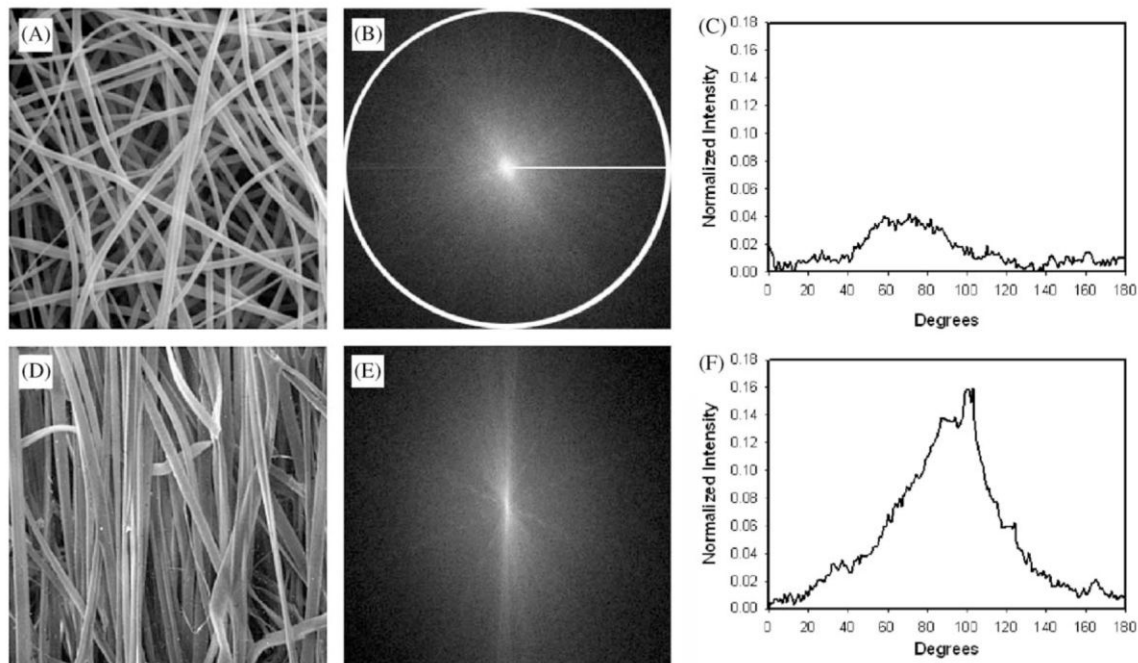
5. *Ayres 2006 (Ex. 1013)*

Ayres 2006 is an article published in *BIOMATERIALS* in 2006 and was later published online at PubMed Central in 2010. Ex. 1013, 1. It names several of the same authors as Ayres 2008, including Petitioner’s expert, Dr. Simpson. As noted above, Huang² cites Ayres 2006 as the source for the FFT methodology used therein. Ex. 1005, 1800. Patent Owner does not dispute that Ayres 2006 qualifies as prior art.

Ayres 2006 describes the use of FFT in the measurement of anisotropy in electrospun scaffolds of gelatin. Ex. 1013, 1. Ayres 2006 notes that, “[b]y using FFT to assign relative alignment values to an electrospun matrix it is possible to systematically evaluate how different processing variables impact the structure and material properties of a scaffold.” *Id.*

Ayres 2006 describes an FFT process, similar to that of Ayres 2008, for quantifying the degree of fiber alignment. As explained in Ayres 2006, “[t]he FFT function converts information present in an original data image from ‘real’ space into mathematically defined ‘frequency’ space,” with “[t]he resulting FFT output image contain[ing] grayscale pixels . . . distributed in a pattern that reflects the degree of fiber alignment present in the original data image.” *Id.* at 3. According to Ayres 2006, “[a] graphical depiction of the FFT frequency distribution can be generated by placing a circular projection on the FFT output image and conducting a radial summation of the pixel intensities for each degree between 0° and 360°, in 1° increments.” *Id.* at 4. Once these summations are obtained, the pixel intensities were plotted between 0° and 180°. *Id.* Ayres 2006 notes that, because “the FFT is symmetric about the horizontal axis[, . . .] a pixel summation to 360° is unnecessary.” *Id.*

Using this methodology, Ayres 2006 presents the results of an FFT analysis for a subjectively judged “random” matrix and an “aligned” matrix in Figure 1, which is reproduced below.



Ex. 1013, 12. Figure 1, reproduced above, shows two rows of three images. The upper row of images depicts, from left to right, a SEM image of a *random matrix* (Fig. 1A), the corresponding FFT output image (Fig. 1B), and the resulting pixel intensity plot (Fig. 1C). *Id.* The lower row of images depicts, from left to right, a SEM image of an *aligned matrix* (Fig. 1D), the corresponding FFT output image (Fig. 1E), and the resulting pixel intensity plot (Fig. 1F). *Id.* As shown above, the FFT output image for the aligned matrix contains pixels distributed in a “non-random, elliptical distribution” compared to the “symmetrical, circular shape” for the FFT output image of the random matrix. *Id.* at 3–4. “This distribution occurs because the pixel intensities are preferentially distributed with a specific orientation.” *Id.* at 4. The pixel intensity plot for the aligned matrix shows a distinct peak around 90°, with the height and overall shape of the peak reflecting the degree of alignment. *Id.*

D. Ground 1: Anticipation by Huang2

In Ground 1, Petitioner contends that claims 1–12 are anticipated by Huang2. Pet. 28–44. As explained below, we find that Petitioner has proven by a preponderance of evidence that Huang2 anticipates claims 1–3 and 5–12, but not that it anticipates claim 4.

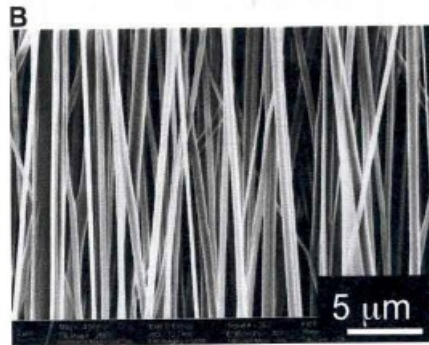
1. Independent Claim 1

Claim 1 requires a “scaffold” comprising “one or more electrospun fibers comprising collagen, wherein a fast Fourier transform (FFT) analysis result of the fibers have adjacent major peaks with about 180° apart from each other.” Ex. 1001, 23:6–9.

With regard to the “scaffold” element, Petitioner cites Huang2’s “scaffolds [that] not only . . . provide a surface for cells to reside, but also . . . define a cell-friendly microenvironment that maximally recaptures the native extracellular matrix (ECM).” Pet. 28 (citing Ex. 1005, 1791). Patent Owner does not dispute that Huang2 discloses a scaffold as argued by Petitioner. PO Resp. 12–29. We are persuaded that Huang2 discloses this claim element.

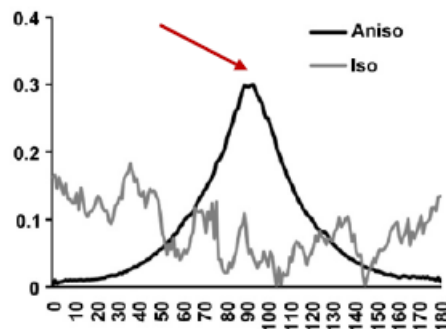
With regard to “electrospun fibers comprising collagen,” Petitioner cites Huang2’s disclosure of forming “[n]anofibrous matrices of PCL and Collagen” by “[e]lectrospinning a blend solution of collagen and polycaprolactone (PCL) [that] can yield rather stable nanofibers.” Pet. 28–29 (citing Ex. 1005, 1791–92). Patent Owner does not dispute that Huang2 discloses electrospun fibers comprising collagen as argued by Petitioner. See PO Resp. 10 (“Huang2 provides an electrospun scaffold made from a blend of collagen and polycaprolactone.”). We agree with Petitioner that this claim element is disclosed by Huang2.

With regard to the recited “FFT analysis result of the fibers hav[ing] adjacent major peaks with about 180° apart from each other,” Petitioner argues that “Huang2 describes PCL/collagen nanofibers that are visually highly aligned with major peaks that are about 180° apart.” Pet. 29. Huang2 Figure 1B is reproduced below.



Ex. 1005, Fig. 1B. Figure 1B, reproduced above, shows a SEM image of an “anisotropic” (aligned) sample. *Id.* at 1793. Patent Owner does not dispute that Huang2 discloses a PCL/collagen nanofibrous matrix of aligned fibers. PO Resp. 11.

Petitioner next points to Huang2’s statement that, “[t]o better analyze the fiber alignment, FFT analysis was performed on [Huang2’s] SEM images . . . to characterize the anisotropy [(i.e., alignment)] and assign a numerical value to fiber orientation.” Ex. 1005, 1794 (cited at Pet. 30). The FFT results of both the aligned and unaligned fibers are plotted in Figure 1C, which is reproduced below, with Petitioner’s annotation.



Pet. 30 (annotating Ex. 1005, Fig. 1C). Figure 1C, reproduced above as annotated by Petitioner, shows the normalized intensity plots against the angle of acquisition, from 0° through 180°, for the aligned (Aniso) and unaligned (Iso) samples obtained using FFT analysis. Ex. 1005, 1793.

Petitioner argues that, for the aligned sample, a major peak occurs at about 90° as identified by Petitioner's annotation (red arrow). Pet. 30–31. As support, Petitioner directs us to Huang2's explicit description of what the peak indicates, namely that "[t]he narrow peak of the normalized intensity values in anisotropic [aligned] matrices (Figure 1C) indicated that *PCL/Coll nanofibers aligned along a single axis* (Fig. 1B)." *Id.* at 31 (alterations in original) (quoting Ex. 1005, 1794). Patent Owner disputes that the illustrated peak is a major peak solely based on the lack of any lesser peaks. *See* PO Resp. 13 ("[T]he height of the sole peak *is identical to*—not higher than—the average height of the peaks in the result."). As discussed above, however, we do not construe "major peaks" as requiring the existence of non-major peaks.

We find that the illustrated peak in the Aniso plot of the FFT analysis results (Figure 1C) is a major peak within the meaning of the claim. The evidence in support of this finding is overwhelming. First, the term "Aniso" as used in Huang2 refers to fibers "with alignment." Ex. 1005, 1792. Huang2 describes fabricating such matrices of aligned fibers with electrospinning, the same method used to impart alignment in the '223 patent. *Id.* at 1791–92. Huang2 visually confirms that the fibers in fact are aligned via scanning electron microscopy. *Id.* at Fig. 1B. Further, Huang2 explicitly states that the peak illustrated in the Aniso plot of the FFT analysis results (Figure 1C) is caused by the fact that the "PCL/Coll nanofibers aligned along a single axis (Fig. 1B)." *Id.* at 1794. This is precisely what

the '223 patent states is to be expected. The '223 patent discloses that electrospinning may yield aligned fibers and images of aligned fibers will yield FFT results with major peaks. Ex. 1001, 2:18–19, 4:46–60, 13:16–26.

Additionally, Huang2 itself considers the peak illustrated in the Aniso plot of the FFT analysis to be *significant*, stating: “In contrast [to the Aniso plot], the lack of a significant peak for the fibers collected on a stationary surface [(i.e., without electrospinning)] demonstrated no preferred fiber orientation in the isotropic matrices” (i.e., the Iso plot). Ex. 1005, 1794. Indeed, the asserted major peak in the Aniso plot shown in Huang2’s Figure 1C is higher than any other data point on the plot.

For these reasons, we find the peak to be a major peak.¹⁵

Petitioner acknowledges that Figure 1C only reports its results through 180°, but contends that “Huang2’s FFT analysis would necessarily show a second major peak at around 270° (which is 180° from the 90° peak) if the scale were extended to 0°–360°.” Pet. 31 (citing Ex. 1010, 609). Petitioner’s evidence on this point is strong. *See* Ex. 1010, 609 (“Typically, the data from this [FFT] analysis is reported for 0 to 180°; the frequency plot is symmetric so a complete summation from 0 to 360° is not technically necessary.”); Ex. 1013, 4 (“the FFT is symmetric about the horizontal axis so a pixel summation to 360° is unnecessary”) (cited at Pet. 10). Indeed, Patent Owner does not dispute that a second and identical peak would exist around 270° if the Aniso plot shown in Huang2’s Figure 1C were extended. *See, e.g.*, PO Sur-Reply 12 (arguing that neither peak is a major peak but not

¹⁵ Although we reject Patent Owner’s construction of “major peaks,” Patent Owner argues that it “reflects real-world scaffolds.” PO Sur-Reply 7; *see also* Tr. 45:10–20. There is no dispute that Huang2’s scaffold that produced the “Aniso” plot in the figure is a real-world scaffold.

disputing that the second peak would occur). These two peaks – at about 90° and 270° – are “about 180° apart from each other,” as recited in claim 1.

We have reviewed both parties’ arguments and evidence, and we find, based on a preponderance of the evidence, that claim 1 is unpatentable as anticipated by Huang2.

2. Dependent Claim 2

Dependent claim 2 recites: “The scaffold according to claim 1, wherein the fibers comprise type I collagen in its native triple helical structure.” Ex. 1001, 23:10–11.

With regard to this claim, Petitioner points to Huang2’s teaching that “type I collagen” was used, and further that type I was well-known and generally understood to have a triple-helical form. Pet. 33 (citing Ex. 1005, 1792; Ex. 1017, 1, 9; Ex. 1003 ¶117). Petitioner also argues, with supporting testimony from Dr. Simpson, that “if the type 1 collagen purchased from a supplier were denatured and/or fragmented (i.e., not in a triple helix) it would be sold as ‘gelatin,’ not ‘collagen.’” *Id.* (citing Ex. 1003 ¶117). Petitioner further argues that Huang2 dissolves its PCL/collagen mixture in HFIP¹⁶, which “was known to stabilize collagen’s triple helix structure.” *Id.* at 33–34 (citing Ex. 1015, 3782). Patent Owner argues to the contrary – that type I collagen denatures from its native triple helical in the presence of HFIP. PO Resp. 30 (citing Ex. 2015 ¶109; Ex. 1005, 1792).

Petitioner replies, in part, with a claim construction argument. In that regard, Petitioner asserts that, although “Claim 2 requires that the fibers

¹⁶ The parties agree that HFIP refers to 1,1,1,3,3,3-hexafluoro-2-propanol. Pet. 33; PO Resp. 30; *see also* Ex. 1016 Ex. 1005, 632 (stating the same).

comprise type 1 collagen in its native triple helical structure,” it “does not require that the collagen remains in its triple helical form *after* being electrospun.” Pet. Reply 16–17. We are not persuaded by Petitioner’s claim construction argument. Claim 2, through its dependence on claim 1, is directed to “[a] scaffold comprising one or more electrospun fibers comprising collagen . . . wherein the fibers comprise type I collagen in its native triple helical structure.” Ex. 1001, 23:6–11. The “fibers” in both claims 1 and 2 refers to fibers that form the scaffold, not raw ingredient fibers before they become part of the claimed invention.

Thus, we are left with the technical dispute as to whether Huang2’s scaffold (matrix) comprises type I collagen in its native triple helical structure. In addition to the evidence cited in the Petition discussed above, Petitioner points out that Patent Owner’s witness, “Dr. Mikos[,] published in the prior art, citing Dr. Simpson, that even after electrospinning using HFIP as a solvent, the electrospun collagen still ‘possessed the typical 67 nm banding pattern observed in *native collagen*.’” Pet. Reply 17 (quoting Ex. 1209, 1205, and citing Ex. 1220, 141:4–142:2; Ex. 1219 ¶45). Patent Owner does not directly address or otherwise rebut this evidence. *See* PO Sur-Reply 17–18.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 2 and thus find claim 2 is unpatentable as anticipated by Huang2.

3. *Dependent Claim 3*

Dependent claim 3 recites: “The scaffold according to claim 1, wherein the fiber has less than about 8 wt % residual calcium.” Ex. 1001, 23:12–13.

With regard to this claim, Petitioner points out that Huang2 does not indicate that any calcium was used when describing the materials used to prepare the nanofibers. Pet. 34 (citing Ex. 1005, 1792).

Patent Owner responds that “Huang2 does not disclose the experimental protocol by which its collagen was isolated, which *may* have involved the use of calcium salts or calcium-containing reagents.” PO Resp. 32 (citing Ex. 2015 ¶117). Patent Owner also argues that “Huang2’s scaffold necessarily includes residual calcium” because they “are grown in a culture medium including ‘10% fetal bovine serum’”(FBS). *Id.* (citing Ex. 1005, 1792). According to Patent Owner, FBS “naturally contains high concentrations of calcium,” some of which “the scaffolds will chelate.” *Id.* at 32–33 (citing Ex. 2015 ¶119). Patent Owner argues that it is Petitioner’s burden to demonstrate that the residual calcium would not exceed the limit recited in claim 3 (i.e., 8 wt %). *Id.* at 33.

In reply, Petitioner labels Patent Owner’s argument “pure speculation.” Pet. Reply 18. And, in sur-reply, Patent Owner responds that Patent Owner’s argument “is less speculative than Petitioner’s,” and that “[t]he burden is Petitioner’s alone, and Petitioner failed.” PO Sur-Reply 19.

It is true that Petitioner bears the burden to prove (by a preponderance of the evidence) that Huang2 anticipates claim 3. On the evidence before us, Petitioner has met this burden by demonstrating that Huang2 does not describe its scaffold’s fiber as containing calcium. Patent Owner presents arguments and evidence that theorize that some amount of calcium would be present in Huang2’s fibers despite Huang2 not mentioning it. Even assuming Patent Owner is correct, Patent Owner does not argue, let alone corroborate, that the residual calcium it theorizes would be present would exceed about 8 wt %.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 3 and thus find claim 3 is unpatentable as anticipated by Huang2.

4. Dependent Claim 4

Dependent claim 4 recites: “The scaffold according to claim 1, wherein the scaffold has an average porosity from about 60% to about 90%.” Ex. 1001, 23:14–15.

With regard to this claim, Petitioner cites Huang 2’s disclosure of “electrospun nanofibrous matrices characterized by ultrafine continuous nanoscaled fibers, high surface-to-volume ratio, *high porosity* and variable pore-size distribution, have great potential to mimic the skin ECM in both morphology and composition.” Pet. 44 (citing Ex. 1005, 1791). Although Huang2 does not specify any numerical percentages for the desired porosity level, Petitioner points out that Huang2 cites Kumbar (reference [3]) with respect the desired characteristics. *Id.* at 44–45 (citing Ex. 1005, 1799). In particular, Petitioner points out that Kumbar discloses that collagen type I has a porosity of 89%, which decreased to 71% when crosslinked. *Id.* at 45 (citing Ex. 1006, 7). However, as Petitioner recognizes, Huang2 does not explicitly disclose the claimed porosity levels.

We are *not* persuaded, based on a preponderance of the evidence, that Huang2 anticipates claim 4.

5. Dependent Claim 5

Dependent claim 5 recites:

The scaffold according to claim 1, wherein the scaffold comprises collagen type I, bone matrix, adipose extracellular matrix, heart basement membrane extract, heart basement membrane extracellular matrix, placenta basement membrane extract, placenta basement membrane extracellular matrix,

brain-derived extracellular matrix, polycaprolactone, an accessory polymer, or the mixture thereof.

Ex. 1001, 23:16–22.

With regard to this claim, Petitioner points to Huang2’s teaching that the scaffold can be made of a mixture of polycaprolactone (PCL) and type I collagen. Pet. 36 (citing Ex. 1005, 1792). Petitioner further points out the PCL disclosed in Huang2 qualifies as an “accessory polymer” (as defined in the ’223 patent) because it is used to improve the stability and mechanical properties of the fibers. *Id.* at 36–37 (citing Ex. 1005, 1791–92). Patent Owner does not present any separate arguments for dependent claim 5.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 5 and thus find claim 5 is unpatentable as anticipated by Huang2.

6. Dependent Claim 6

Dependent claim 6 depends from claim 5 and specifies that the “accessory polymer” is selected from a *Markush* group recited therein, a member of which is polycaprolactone (PCL). Ex. 1001, 23:23–37.

With regard to this claim, Petitioner points to Huang2’s disclosure of PCL as an accessory polymer. Pet. 37 (citing Ex. 1005, 1792). Patent Owner does not present any separate arguments for dependent claim 6.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 6 and thus find claim 6 is unpatentable as anticipated by Huang2.

7. Dependent Claim 7

Dependent claim 7 recites: “The scaffold according to claim 1, wherein the scaffold comprises a bioactive factor.” Ex. 1001, 23:38–39.

With regard to this claim, Petitioner points to Huang’s disclosure of collagen, which is identified in the ’223 patent as an exemplary “bioactive factor.” Pet. 38 (citing Ex. 1001, 12:44–67; Ex. 1005, 1792). Patent Owner does not present any separate arguments for dependent claim 7.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 7 and thus find claim 7 is unpatentable as anticipated by Huang2.

8. Dependent Claim 8

Dependent claim 8 depends from claim 7 and specifies that the “bioactive factor” is selected from a *Markush* group recited therein, a member of which is collagen. Ex. 1001, 23:40–24:13.

With regard to this claim, Petitioner points to Huang2’s disclosure of collagen as a bioactive factor. Pet. 39–40. Patent Owner does not present any separate arguments for dependent claim 8.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 8 and thus find claim 8 is unpatentable as anticipated by Huang2.

9. Dependent Claim 9

Dependent claim 9 recites: “The scaffold according to claim 1, wherein the scaffold comprises an extracellular matrix component.” Ex. 1001, 24:14–15.

With regard to this claim, Petitioner points to Huang2’s disclosure of collagen as the extracellular matrix (ECM) component. Pet. 40–41. Petitioner points out that Huang2 teaches that “[c]ollagen fibrils” are a “major ECM component known for their mechanical contribution to skin integrity, and that electrospun collagen fibers were fabricated “[t]o better

mimic skin ECM.” *Id.* (citing Ex. 1006, 1791). Patent Owner does not present any separate arguments for dependent claim 9.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 9 and thus find claim 9 is unpatentable as anticipated by Huang2.

10. Dependent Claim 10

Dependent claim 10 depends from claim 9 and specifies that the “extracellular matrix component” is selected from a *Markush* group recited therein, a member of which is collagen. Ex. 1001, 24:16–20.

With regard to this claim, Petitioner points to Huang2’s disclosure of collagen as the extracellular matrix component. Pet. 41. Patent Owner does not present any separate arguments for dependent claim 10.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 10 and thus find claim 10 is unpatentable as anticipated by Huang2.

11. Dependent Claim 11

Dependent claim 11 recites: “A method of cell culture comprising culturing cells on the scaffold according to claim 1 under conditions suitable for the cell culture.” Ex. 1001, 24:21–23.

With regard to this claim, Petitioner points to Huang2’s teaching of culturing fibroblasts (NHDFs) on anisotropic nanofibrous matrices for up to 7 days. Pet. 42 (citing Ex. 1005, 1792). Petitioner also points to Huang2’s teaching of a wound healing assay, the results of which are shown in Figure 6 depicting the migration of human dermal fibroblasts on PCL/Coll nanofibrous matrixes. *Id.* at 42–43 (citing Ex. 1005, 1797 (Fig. 6A)). Patent Owner does not present any separate arguments for dependent claim 11.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 11 and thus find claim 11 is unpatentable as anticipated by Huang2.

12. Dependent Claim 12

Dependent claim 12 depends from claim 11 and specifies that the type of “cells” are selected from a *Markush* group recited therein, a member of which is fibroblasts. Ex. 1001, 24:24–26.

With regard to this claim, Petitioner points to the disclosure in Huang2 about culturing fibroblasts on the nanofibrous matrices. Pet. 43–44 (citing Ex. 1005, 1792). Patent Owner does not present any separate arguments for dependent claim 12.

We are persuaded, based on a preponderance of the evidence, that Huang2 discloses the additional limitation recited in claim 12 and thus find claim 12 is unpatentable as anticipated by Huang2.

E. Ground 2: Obviousness of Claim 4 Over Huang2 and Kumbar

Dependent claim 4 specifies that “the scaffold has an average porosity from about 60% to about 90%.” Above, we determined that Petitioner failed to prove that Huang2 anticipates claim 4. Ex. 1001, 23:14–15; *see supra*. In Ground2, Petitioner contends that claim 4 would have been obvious over the combination of Huang2 and Kumbar. Pet. 44–47.

As discussed above, Huang2 discloses “high porosity” among the desirable characteristics of the electrospun nanofiber matrices. Ex. 1005, 1791. Although Huang2 does not directly quantify “high porosity,” it cites Kumbar as a reference in support of this feature. *Id.* at 1791, 1799 (reference [3]). Kumbar discloses methods of designing electrospun

nanofiber matrix scaffolds “to provide cells with the necessary chemical cues and a more in vivo like environment” for use “in the regeneration of various soft tissues including skin.” Ex. 1006, 1 (Abstract). Kumbar also states that a “high porosity” is desirable for these matrices as that property more closely approximates the natural ECM. *Id.* In terms of the specific amount of porosity, Petitioner points to Kumbar’s disclosure that collagen type I fibers had a porosity of 89%. *Id.* at 7. Kumbar also indicates that it can be useful to cross-link collagen type I nanofibers and that such crosslinked fibers were similar in strength to certain commercially available wound care products. *Id.* However, when these fibers were cross-linked, the porosity decreased to 71%. *Id.*

Petitioner contends that a person of ordinary skill in the art “who desired to make aligned collagen blended fibers (as taught by Huang2) with ‘high porosity’ (as also taught by Huang2) would have been motivated to look at the reference cited by Huang2 in support of the ‘high porosity.’” Pet. 45–46 (citing Ex. 1003 ¶169). Accordingly, Petitioner contends that there would have been strong motivation to look to Kumbar’s teachings that collagen fiber scaffolds have a porosity of 89% (or 71% if crosslinked). *Id.* at 46 (citing Ex. 1006, 1, 6–7, 12; Ex. 1003 ¶169). Petitioner contends that both Huang2 and Kumbar are in the same field, involving the use of electrospun collagen-containing scaffolds for biomedical applications such as skin grafts. *Id.* (citing Ex. 1005, 1791; Ex. 1006, 1; Ex. 1003 ¶170). Petitioner also contends, based on Dr. Simpson’s testimony, that a person of ordinary skill in the art would know how to tailor the porosity of electrospun fibers using well-known methods such as freeze-drying, salt leaching, and gas foaming. *Id.* at 46–47 (citing Ex. 1003 ¶171).

In response, Patent Owner contends that a person of ordinary skill in the art “would not have expected success in modifying Huang2 to reflect Kumbar’s porosities.” PO Resp. 38. This, according to Patent Owner, is because Huang2 and Kumbar use different electrospinning parameters, including different polymers, with Huang2 using a 3:1 blend of PCL and collagen and Kumbar using pure collagen or cross-linked pure collagen. *Id.* at 36 (citing Ex. 1005, 1792; Ex. 1006, 8; Ex. 2015 ¶132). Patent Owner argues that, “[b]ecause the electrospinning polymers differ, the electrospinning solution properties—and consequently the porosities—of Huang2 and Kumbar also necessarily differ.” *Id.* at 37 (citing Ex. 2015 ¶133; Ex. 2017, 42:18–43:4). Indeed, Dr. Simpson agreed during cross-examination that “certainly electrospinning conditions affect porosity,” including “polymer molecular weight and polymer solution properties.” Ex. 2017, 42:18–43:4.

In reply, Petitioner points out the lack of teaching within the ’223 patent as to how to obtain the recited range of porosities, thereby implying that a person of ordinary skill in the art would understand how to obtain such ranges based on the prior art. Pet. Reply 18–19; *see Uber Techs., Inc. v. X One, Inc.*, 957 F.3d 1334, 1339 (Fed. Cir. 2020) (“The specification of the ’593 patent is entirely silent on how to transmit user locations and maps from a server to a user’s mobile device, suggesting that a person of ordinary skill in the art was more than capable of selecting between the known methods of accomplishing this.”). Petitioner also provide numerous evidentiary citations showing that it was known (1) that fiber size affects porosity and (2) how to adjust fiber size by adjusting electrospinning parameters. Pet. Reply. 19 (citing Ex. 1214, 7; Ex. 1220, 148:9–19; Ex. 2017, [44:]16–18; Ex. 1006, 2; Ex. 1215, 2800, Tables 1–2; Ex. 1219

¶54); *see also* Ex. 2017, 44:16–18 (Dr. Simpson testifying on cross-examination that the most important factor determining porosity is fiber size). Further, Kumbar states that electrospinning “is simple, elegant, reproducible, continuous and scalable” and makes it “possible to fabricate fibers in the diameter range of ~3nm–6µm and several meters in length using the same experimental set-up.” Ex. 1006, 2; *see also id.* (“[I]ncrease in viscosity or polymer concentration results in fiber diameter increase. By changing polymer concentration alone it is possible to fabricate the fiber diameters in the range of few nm to several micrometers while keeping other electrospinning parameters at a constant.”).

In its Sur-Reply, Patent Owner maintains that the proposed modification of Huang2 in view of Kumbar would not work given the different parameters they use. PO Sur-Reply 20–21. Patent Owner also argues that adjusting the electrospinning parameters also would not work and, in any event, is a new and improper argument on reply. *Id.* at 21–22.

We disagree that Petitioner’s argument regarding adjusting the electrospinning parameters is improper. The Petition set forth a *prima facie* case of obviousness based on Huang2 and Kumbar, including an assertion of reasonable expectation of success supported by evidence. *See* Pet. 46–47; Ex. 1003 ¶171. Petitioner’s “new” argument about adjusting the electrospinning parameters properly replies to Patent Owner’s arguments. *See, e.g.*, PO Resp. 36 (“A POSITA would not expect to achieve Kumbar’s high porosity levels in Huang2’s scaffold *given the notably different electrospinning parameters used in each reference.*” (emphasis added)).

We are persuaded by Petitioner’s arguments and evidence that claim 4 would have been obvious over Huang2 and Kumbar.

First, the law requires not absolute success, as Patent Owner’s arguments might imply,¹⁷ but rather a *reasonable* expectation of success. *See In re O’Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988) (“Obviousness does not require absolute predictability of success. . . . For obviousness under § 103, all that is required is a reasonable expectation of success.”). “Reasonable expectation of success is assessed from the perspective of the person of ordinary skill in the art,” and “is a question of fact.” *Life Techs. Inc. v. Clontech Labs. Inc.*, 224 F.3d 1320, 1326 (Fed. Cir. 2000); *Medichem S.A. v. Rolabo S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006).

Here, we find there would have been a reasonable expectation of success. The prior art and testimony before us demonstrate that a person of ordinary skill in the art readily understood the factors that affect porosity and knew how to alter them to achieve desired porosities. Indeed, the ’223 patent implies as much by omitting any teaching as to how to obtain the recited porosity range.

In its Sur-Reply, Patent Owner further argues that “Petitioner’s Reply addresses whether a POSITA *could have* modified electrospinning parameters. . . . It does not sufficiently address *why* a POSITA would have done so.” PO Sur-Reply 22. This argument is inapposite because *the Petition* adequately addressed the “why.” *See* Pet. 45–46 (“[A] POSA who desired to make aligned collagen blended fibers (as taught by Huang2) with ‘high porosity’ (as also taught by Huang2) would have been motivated to

¹⁷ *See* PO Resp. 36 (“[A] POSITA would not have expected success in utilizing Kumbar’s porosity in Huang2’s scaffold for several reasons.”), 38 (“[A] POSITA would not have expected success in modifying Huang2 to reflect Kumbar’s porosities.”), 38–39 (“A POSITA would not have expected success in modifying Huang2’s scaffold to possess the porosity disclosed by Kumbar.”).

look at the reference cited by Huang2 in support of the ‘high porosity.’” (citing Ex. 1003 ¶169)), 46 (“Huang2’s and Kumbar’s discussion of the benefits of mimicking the porosity of the native skin ECM would have further motivated a POSA to combine the teachings of Kumbar modify Huang2’s disclosed scaffolds to have porosity of 89% or 71%.”). Notably, the Patent Owner Response did not challenge Petitioner’s reasoning for why a person of ordinary skill in the art would have combined Huang2 and Kumbar; it only challenged whether the skilled artisan would have been successful (although, again, the legally relevant issue is whether there would have been a *reasonable* expectation of success). PO Resp. 36–39.

We have reviewed both parties’ arguments and evidence, and we determine, based on a preponderance of the evidence, that claim 4 is unpatentable as it would have been obvious over Huang2 and Kumbar.

F. Ground 3: Anticipation by Lee

In Ground 3, Petitioner contends that claims 1–12 are anticipated by Lee. Pet. 47–64. As explained in our analysis below, we find that Petitioner has failed to prove by preponderance of evidence that Lee anticipates claims 1–12.

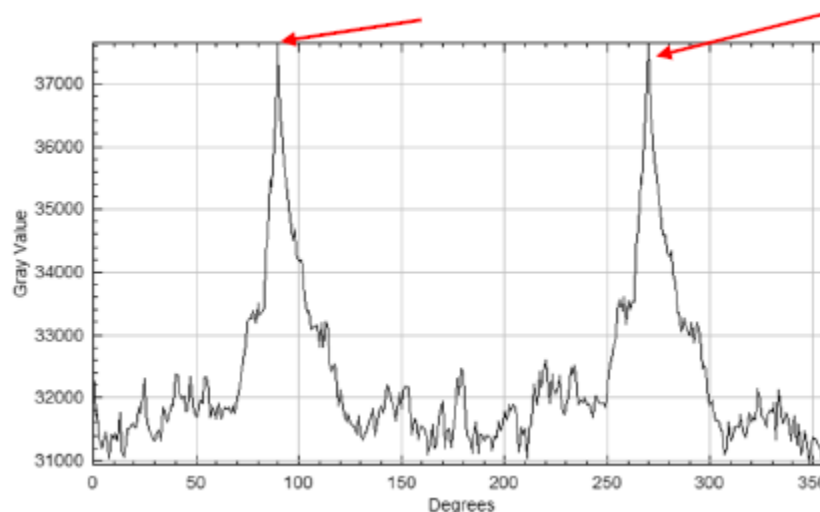
Regarding the “scaffold” requirement, Lee teaches “a biodegradable scaffold comprising a plurality of fibers oriented along a longitudinal axis.” Ex. 1011, Abstr.; *see also* Pet. 47–48 (identifying teachings in Lee for a “scaffold”). Patent Owner does not dispute that Lee discloses a scaffold as argued by Petitioner. PO Resp. 39–58. We are persuaded that Lee discloses this claim element.

Regarding the requirement for “one or more electrospun fibers comprising collagen,” Lee discloses “electrospun PCL/collagen nanofibers.” Ex. 1011 ¶11; *see also* Pet. 48–49 (identifying teachings in Lee related to electrospinning fibers to form PCL-collagen composite scaffolds). Patent Owner does not dispute that Lee discloses electrospun fibers comprising collagen as argued by Petitioner. PO Resp. 39–58. We are persuaded that Lee discloses this claim element.

Regarding the requirement that the fibers exhibit an FFT analysis result having “adjacent major peaks with about 180° apart,” Petitioner does not assert that Lee discloses an FFT analysis of its fibers; Lee does not. Petitioner, however, points to other teachings in Lee with regard to studying the impact of alignment and orientation of the electrospun PCL/collagen nanofibers on the performance and properties of the scaffolds. Pet. 49–52. In particular, Lee discloses that “[f]iber orientations were induced by electrospinning onto a collector at different rotation rates.” Ex. 1011 ¶61. Lee analyzed SEM images of the scaffolds with the “UTHSCSA ImageTool 3.0” to determine the average fiber diameters and fiber orientations within the nanofiber meshes. *Id.* ¶66. Because the SEM images in Lee have poor image quality, Petitioner points to images from Lee’s provisional application serial no. 61/025,350 (“Lee’s provisional application”; Ex. 1021) as showing the same data, but with clearer images. Pet. 50–51; *see* Ex. 1021, 38 (Figs. 1D, 1H). Petitioner contends that the image analysis from the figures in Lee’s provisional application show that Lee discloses highly aligned fibers. Pet. 52.

Although Lee does not disclose an FFT analysis, Petitioner contends that a POSITA “would know that the degree of alignment could also be determined using ImageJ software to run an ‘FFT analysis.’” *Id.* Petitioner

contends that such an application of the ImageJ software was well known at the time of Lee's filing, and the use of such an FFT analysis would confirm fiber alignment. *Id.* Petitioner further points to Dr. Simpson's own FFT analysis based on Figure 1D of Lee's provisional, which produced the following plot:



Pet. 53. Dr. Simpson explains that he conducted his own analysis of Lee's Figure 1D using the FFT methodology identified in the '223 patent (based on the Ayres 2008 paper), and reported the data from 0° to 360° as shown above. Ex. 1003 ¶188. As explained by Dr. Simpson, the graph above demonstrates that the aligned fibers have a first major peak at about 90° and a second major peak at about 270° (annotated with red arrows), which shows the peaks are about 180° apart as recited in claim 1. *Id.* ¶189.

Patent Owner argues that (1) Petitioner's anticipation arguments about what a theoretical FFT analysis result might show in regards to Lee's scaffold are "unclear" and (2) Dr. Simpson's FFT analysis was faulty and is "entitled to no weight." PO Resp. 39, 44.

Relevant to Patent Owner's first point, the Institution Decision stated the following:

Petitioner does not clearly assert in the Petition that the fibers taught by Lee necessarily or inherently satisfy the FFT analysis requirement. Rather, Petitioner only asserts that “it was well known at the time of filing that an FFT analysis *could be* performed to further confirm alignment,” and “[t]his *would show* the fibers were oriented on the scaffold in Lee in an aligned manner.” Petitioner’s grounds based on Lee may ultimately fail on the merits due to this lack of specificity.

Inst. Dec. 37 (quoting Pet. 52). We agree with that initial analysis—that the Petition does not assert that the fibers taught by Lee necessarily or inherently satisfy the FFT analysis requirement.

In its Reply, Petitioner attempts to persuade us otherwise, asserting that “the Petition specifically asserts inherency.” Pet. Reply 22. According to Petitioner:

The Petition asserts that performing an FFT analysis on Lee’s fibers “would show” that the fibers are aligned, and the Petition then presents an FFT analysis that confirms “adjacent major peaks at around 90° and 270°.” (Paper-2, 52.) The phrase “would show” indicates that the claimed peaks are a necessary result of performing an FFT analysis on Lee’s fibers. *See Arbutus Biopharma Corporation v. ModernaTX, Inc.*, 65 F.4th 656, 662 (Fed. Cir. 2023) (explaining that the standard for inherent anticipation is whether the practice of the prior art “would result in the claimed product.”) This portion of the Petition further cites Dr. Simpson, who stated in his declaration that the FFT peaks obtained by his testing “are a natural and necessarily present property of the fibers that Lee discloses,” which is the hallmark for inherency. (EX1003, ¶190 (incorporated into Paper-2, 52).)

Id. Petitioner is combining arguments that were presented separately in the Petition about, on the one hand, what a theoretical FFT analysis result that “could be performed” would show and, on the other hand, what Dr. Simpson’s FFT analysis result purportedly shows.

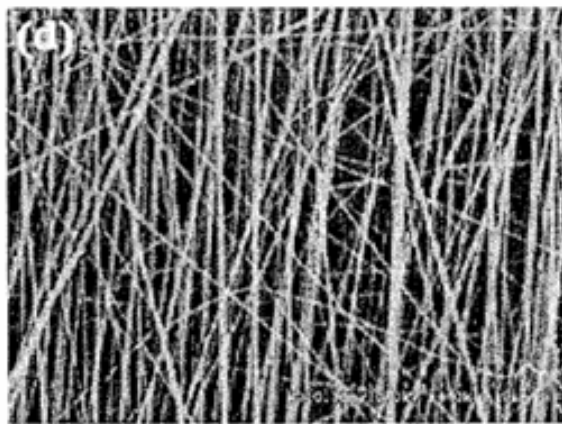
First, the Petition uses the phrase “would show” in reference to an FFT analysis result showing aligned fibers, not in reference to an FFT analysis result having adjacent major peaks with about 180° apart from each other. *See* Pet. 52 (“[I]t was well known at the time of filing of Lee that a FFT analysis *could be performed* to further confirm alignment. (*See* EX1010). *This would show the fibers were oriented on the scaffold in Lee in an aligned manner.*” (emphasis added)). Second, Petitioner’s argument that “the Petition then presents an FFT analysis that confirms ‘adjacent major peaks at around 90° and 270°’” (Pet. Reply 22 (quoting Pet. 52)) is referring to what Dr. Simpson’s FFT analysis result purportedly shows; it is not referring to the theoretical FFT analysis that Petitioner separately argues “could be performed to further confirm alignment.” Pet. 52.

Nowhere *in the Petition* does Petitioner argue that the FFT analysis result of Lee’s fibers that “could be performed” (*see* Pet. 52) necessarily or inherently would have major peaks with about 180° apart from each other. This is not to say that the evidence of record could not support such an assertion. In fact, it clearly does, as Lee disclosed a scaffold of aligned fibers. But the Petition did not assert inherent disclosure of the FFT limitation with particularity. *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (“In an IPR, the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.”); 35 U.S.C. § 312(a)(3) (requiring that “the petition identifies in writing and *with particularity*, each claim challenged, the grounds on which the challenge to each claim is based”) (emphasis added).

We turn now to Petitioner’s theory of anticipation based on the results of Dr. Simpson’s actually performed FFT analysis. Petitioner argues that its “expert, Dr. Simpson, ran an FFT analysis on Figure 1D from Lee’s

provisional, which has the same data as Figure 1D from Lee, and is clearer.” Pet. 52. The resulting graph is included on page 53 of the Petition and is reproduced *supra*. It shows major peaks with about 180° apart from each other. Pet. 52; *see also* Ex. 1003 ¶¶188–189 (Dr. Simpson reproducing and interpreting the graph).

Patent Owner argues that Dr. Simpson’s testing was “plainly inconsistent with ‘the FFT analysis described in the ’223 patent.’” PO Resp. 44 (quoting Ex. 2015 ¶146). In particular, Patent Owner argues that “Dr. Simpson did *not* test high quality images of the type he typically analyzes” and instead used “a remarkably poor-quality photocopy of Lee’s SEM image, shown below (which did not even come from Lee, but instead from Lee’s provisional application).” *Id.* The SEM image from Lee’s provisional application is reproduced below.



Ex. 1021, 38 (Fig. 1D). Figure 1D, reproduced above, is the image Dr. Simpson used for his FFT analysis. Ex. 1003 ¶184. Patent Owner argues that, “[i]mmediately apparent from visual inspection of this image is its poor quality with a facial lack of contrast between individual fibers, especially among fibers toward the background of Lee’s scaffold.” PO Resp. 45. Patent Owner’s witness, Dr. Mikos, testifies that “[a] POSITA would never conduct FFT analysis on such an image. . . . Absent clear delineation

between fibers, especially regarding deeper fibers, the FFT analysis incorrectly analyzes the orientation of the fiber scaffold.” *Id.* (alteration in original) (quoting Ex. 2015 ¶151).

During cross-examination, Dr. Simpson confirmed that he used a photocopy of Figure 1D from Lee’s provisional application.

Q. What was your first step in performing FFT analysis on the Lee provisional Figure 1-D?

A. I selected my square from the middle of the rectangle, trimmed the image, and then conducted the FFT

Q. So you didn’t do your FFT analysis on the actual image that Lee captured with SEM, did you?

A. That was not available to me.

Q. So what you analyzed was a Xerox or a photocopy?

A. This image, yes.

Q. Okay. So it was a photocopy?

A. It was this photocopy.

Ex. 2017, 156:16–157:4. Dr. Simpson further testified that he does not normally do FFT analyses using photocopied images and does not advise his students to do so either. *Id.* at 157:8–158:3.

The fact that Dr. Simpson employed Figure 1D from Lee’s provisional application as opposed to Figure 1D from Lee itself suggests that he agrees that poor image quality is detrimental to an accurate FFT analysis. Figure 1D of Lee’s provisional application, although of better quality than that of Lee itself, nonetheless appears to be of fairly poor quality. Indeed, Dr. Simpson used it “out of necessity.” *Id.* at 157:10–12.

In its Reply, Petitioner argues that “Dr. Simpson has shown that even large amounts of noise do not stop an FFT from demonstrating the claimed FFT peaks if the fibers are in fact aligned.” Pet. Reply 23 (citing Ex. 1219,

¶¶63–64). Patent Owner argues that the cited declaration testimony, which was submitted with the Reply, “is belied by earlier statements.” PO Sur-Reply 26. For example, Patent Owner points out that Ayres 2008, co-written by Dr. Simpson, states that images “composed largely of optical noise . . . are unsuitable for [FFT] analysis.” *Id.* (quoting Ex. 1010, 605). Patent Owner also points out that Ayres 2006, also co-written by Dr. Simpson, states that “noise can degrade the absolute alignment value assigned to a scaffold by FFT analysis.” *Id.* (quoting Ex. 1013, 7).

It is clear from the record before us that image quality is important and that too much noise can render an FFT analysis unreliable. It is not, however, clear how much noise is too much noise. That said, it is Petitioner’s burden to prove unpatentability; it is not Patent Owner’s burden to prove the opposite. Based on the evidence of record, we find that Petitioner has not met its burden given the irregular nature of Dr. Simpson’s FFT analysis (using a photocopy of a SEM image that bears significant noise).

Accordingly, we are *not* persuaded, based on a preponderance of the evidence, that Lee anticipates any of claims 1–12.

G. Ground 4: Obviousness over Lee

In Ground 4, Petitioner contends that claims 1–12 would have been obvious Lee. Pet. 64–66. In doing so, Petitioner relies on the same analysis as provided in Ground 3 but adds that “there would have been motivation and a reasonable expectation of success for a POSA to run an FFT on the aligned fibers fabricated in Lee.” *Id.* at 64. However, as we stated above, nowhere *in the Petition* (be it Ground 3 or Ground 4) does Petitioner argue

that an FFT analysis result of Lee's fibers necessarily or inherently would have major peaks with about 180° apart from each other.

Accordingly, based on a preponderance of the evidence, Petitioner has not shown that any of claims 1–12 would have been obvious over Lee.

III.CONCLUSION

A preponderance of the evidence shows that claims 1–12 are unpatentable. In summary:

Claim(s)	35 U.S.C. §	Reference(s)/Basis	Claim(s) Shown Unpatentable	Claim(s) Not Shown Unpatentable
1–12	102	Huang2	1–3, 5–12	4
4	103	Huang2, Kumbar	4	
1–12	102	Lee		1–12
1–12	103	Lee		1–12
Overall Outcome			1–12	

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 1–12 of U.S. Patent No. 10,137,223 B2 are unpatentable; and

FURTHER ORDERED that 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.

IPR2025-00248
Patent 10,137,223 B2

FOR PETITIONER:

Howard Levine
Jennifer Swan
HOGAN LOVELLS US LLP
howard.levine@hoganlovells.com
jennifer.swan@hoganlovells.com
david.feigenbaum@hoganlovells.com

FOR PATENT OWNER:

Amanda Wieker
Tyler VanHoutan
George Davis
MCGUIREWOODS LLP
awieker@mcguirewoods.com
tvanhoutan@mcguirewoods.com
gdavis@mcguirewoods.com
LNH_IPRS@mcguirewoods.com