

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

EMBODY, INC. AND ZIMMER BIOMET HOLDINGS, INC.,
Petitioners

v.

LIFENET HEALTH,
Patent-Owner.

Case IPR2025-00248
U.S. Patent No. 10,137,223

REPLY TO PATENT-OWNER'S RESPONSE

Filed on behalf of Petitioner

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PETITIONERS' LIST OF EXHIBITS

Exhibit No.	Description	Previously Submitted
1001	U.S. Patent No. 10,137,223 to Francis et al. (“the ’223 patent”)	x
1002	’223 Patent Prosecution History	x
1003	Declaration of David G. Simpson, Ph.D.	x
1004	CV of David G. Simpson, Ph.D.	x
1005	Huang et al., <i>The involvement of integrin $\beta 1$ signaling in the migration and myofibroblastic differentiation of skin fibroblasts on anisotropic collagen-containing nanofibers</i> , 33 Biomaterials 1791-1800 (Feb. 2012) (“Huang2”) (available online Dec. 2, 2011)	x
1006	Kumbar et al., <i>Electrospun nanofiber scaffolds: engineering soft tissues</i> , Biomed. Mater. 3 (2008) (“Kumbar”)	x
1007	Reserved	
1008	Huang et al., <i>Electrospun collagen-chitosan-TPU nanofibrous scaffolds for tissue engineered tubular grafts</i> , 82 Colloids and Surfaces B: Biointerfaces 307-315 (2011) (“Huang1”)	x
1009	U.S. Patent App. Pub. No. 2004/0037813 to Simpson et al. (“Simpson”)	x
1010	Ayres et al., <i>Measuring fiber alignment in electrospun scaffolds: a user’s guide to the 2D fast Fourier transform approach</i> , 19 J. Biomater. Sci. Polymer. 603-621 (2008) (“Ayres2008”)	x
1011	Lee et al., U.S. Patent Application No. US 2010/0331980 A1, Pub. Date December 1, 2011 (“Lee”)	x
1012	Reserved	
1013	Ayres et al., <i>Modulation of Anisotropy in Electrospun TissueEngineering Scaffolds: Analysis of Fiber Alignment by the Fast Fourier Transform</i> , 27(32) Biomaterials 5524-5534 (2006) (“Ayres 2006”)	X
1014	U.S. Pat. No. 5,514,378 to Mikos (“Mikos”)	x
1015	Jose et al, <i>Fabrication and Characterization of Aligned Nanofibrous PLGA/Collagen Blends as Bone Tissue Scaffolds</i> , 50 Polymer 3778-85 (2009) (“Jose”)	x

1016	Fu et al, <i>Spatial Arrangement of Polycaprolactone/Collagen Nanofiber Scaffolds Regulates the Wound Healing Related Behaviors of Human Adipose Stromal Cells</i> , 18(5) Tissue Engineering, 631-42 (2012) (“Fu”)	x
1017	Shoulders & Raines, <i>Collagen Structure and Stability</i> , 78 Annu. Rev. Biochem. 929 (2009)	x
1018	Kuo et al., U.S. Patent Application No. US 2011/0293685 A1, Pub. Date Dec. 1, 2011 (“Kuo”)	x
1019	Beachley et al, <i>Highly Aligned Polymer Nanofiber Structures: Fabrication and Applications in Tissue Engineering</i> (2011) in Vol. 246 Biomedical Applications of Polymeric Nanofibers (Jayakumar & Nair eds. 2011)	x
1020	Declaration of Emma Xu	x
1021	U.S. Provisional Patent App. No. 61/0255,35 (“Lee Provisional”)	x
1022	Reserved	
1023	Reserved	
1024	June 21, 2022 Memo From Katherine Vidal on Interim Procedure for Discretionary Denials in AIA Post-Grant Proceedings with Parallel District Court Litigation (June 21, 2022), available at https://www.uspto.gov/sites/default/files/documents/interim_proc_discretionary_denials_aia_parallel_district_court_litigation_memo_20220621_.pdf	x
1100	<i>LifeNet Health v. Zimmer Biomet Holdings, Inc.</i> , 23-cv-00479, D.I. 41 (10/09/24)	x
1101	ZIMMER BIOMET, <i>Patent Marking List for Website Q1-2025</i> , Last updated Mar. 19, 2025, available at https://www.zimmerbiomet.com/content/dam/zbcorporate/en/corporate/patents/Patent-Marking-Listfor-Website-Q1-2025.pdf (last visited Sept. 9, 2025)	x
1203	Smoak et al, <i>Bioinspired Electrospun dECM Scaffolds Guide Cell Growth and Control the Formation of Myotubes</i> , 7(20) Sci Adv at 1 (May 2021)	
1204	Reserved	
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1206	Reserved	
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1208	Reserved	
1209	Pham et al, <i>Electrospinning of Polymeric Nanofibers for Tissue Engineering Applications: A Review</i> , 12(5) Tissue Engineering 1197 (2006)	
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1211	Subramanian et al, <i>Fabrication of Uniaxially Aligned 3D Electrospun Scaffolds for Neural Regeneration</i> , 6(2) Biomed. Mater. 1 (2011)	
1212	Sell et al, Scaffold Permeability as Means to Determine Fiber Diameter and Pore Size of Electrospun Fibrinogen, 85(1) J. Biomed Mater Res A 115 (2008)	
1213	Meng et al, <i>Electrospinning of PLGA/Gelatin Randomly-Oriented and Aligned Nanofibers as Potential Scaffold in Tissue Engineering</i> , 30(8) Materials Science and Engineering C 1204 (2010)	
1214	Srinivasan et al, <i>Multiscale Fibrous Scaffolds in Regenerative Medicine</i> , 246 Adv Polym Sci 1 (2012)	
1215	Pham et al, <i>Electrospun Poly(ϵ-caprolactone) Microfiber and Multilayer Nanofiber/Microfiber Scaffolds: Characterization of Scaffolds and Measurement of Cellular Infiltration</i> , 7(10) Biomacromolecules 2796 (2006)	
1216	Reserved	
1217	Liu et al, <i>Myoblast Therapy: From Bench to Bedside</i> , 15 Cell Transplantation 455 (2006)	
1218	Reserved	
1219	Declaration of David G. Simpson, Ph.D.	
1220	Transcript of January 21, 2026 Deposition of Dr. Antonios G. Mikos	
1221	Reserved	
1222	Excerpt from Google Scholar, https://scholar.google.com/scholar?hl=en&as_sdt=0%2C47&q=ayres+2008+fft&btnG= (last visited, 2/2/2026)	
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I. INTRODUCTION

The asserted claims of U.S. Patent No. 10,137,223 (“the ’223 patent”) are anticipated and, at minimum, rendered obvious by the prior art. The primary references, Huang² and Lee, which were never considered during prosecution, establish that aligned collagen fibers were well-known long before the alleged invention date of the ’223 patent. The claimed subject matter therefore reflects no inventive contribution by Patent Owner.

Unable to reconcile the claims with this undisputed prior art, Patent Owner retreats from its original position that a reference disclosing only a single FFT peak is insufficient. In its place, Patent Owner now advances a newly minted claim construction that purportedly requires a minimum of four FFT peaks to calculate an average and establish fiber alignment. This construction was never raised during prosecution, related litigation, or in Patent Owner’s Preliminary Response (“POPR”), and appears for the first time only after Petitioner demonstrated that the prior art discloses aligned fibers.

This belated theory rests on improper lexicography arguments and unsupported expert testimony. Patent Owner’s expert has never performed an FFT analysis resulting in alignment plot and could not identify any publication requiring more than two peaks to determine alignment. Nothing prevented Patent

Owner from raising this theory earlier. Its emergence now underscores that it is a litigation-driven attempt to avoid the plain disclosures of Huang² and Lee.

Under this newly advanced construction, Patent Owner asserts that the claims are not directed to aligned collagen fibers, but instead to fibers exhibiting a particular FFT pattern that allegedly requires more than two peaks. Yet neither the '223 patent, Ayres²⁰⁰⁸, the prosecution history, nor any cited prior art discloses such a calculation or requirement. Patent Owner's position thus depends entirely on an analytical framework that appears nowhere in the intrinsic or extrinsic record.

Even applying this unsupported construction, Patent Owner's arguments fail. Patent Owner contends that Huang² discloses only two major peaks and therefore falls outside the claims. That contention is illogical and would improperly sweep within the claims the very embodiment that the specification itself identifies as depicting random fibers outside the claims. Notably, even Patent Owner's expert could not identify a single reference requiring minor peaks to determine major peaks, and a person of ordinary skill in the art would understand that two symmetrical peaks are the hallmark of aligned fibers.

Patent Owner's revised claim construction and the arguments built upon it should therefore be rejected, and the challenged claims should be held unpatentable over the cited prior art.

II. ARGUMENT

A. Huang2 Anticipates Claims 1-3 and 5-12

1. Huang2 Discloses Two Major Peaks in the FFT

The Petition established that Huang2 expressly discloses the claimed FFT requirement of major peaks approximately 180° apart. In its POPR, Patent-Owner argued that Huang2 fails to meet this limitation because the FFT plot displays data only through 180 degrees and therefore shows a single major peak. (Paper-9, 14–16.)

As the Board recognized, that argument is incorrect. (See Paper-14, 24-26.) The results of an FFT plot are symmetrical and only data through 180° need be depicted because a single major peak in the 180° field necessarily shows a symmetrical major peak 180° apart if all 360° were depicted. (Paper-14, 24–26; Paper-2, 22–23, 31.) This principle is expressly disclosed in Ayres2008, which the '223 patent incorporates by reference for FFT analysis. (EX1010, 609; EX1001, 13:16–26.) Patent-Owner cannot contradict statements in its own specification. See *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1362 (Fed. Cir. 2007).

2. Patent-Owner's Claim Construction is Flawed

Recognizing the weakness of its primary position, Patent-Owner now advances a new argument that was absent from its POPR. Patent-Owner proposes a new claim construction that it contends excludes Huang2 as invalidating prior art.

(Paper-24, 6–9, 12–13.) Patent-Owner asserts that the term “major peaks” is expressly defined in the ’223 patent and that the patentee acted as its own lexicographer. Patent-Owner relies on the statement that “[t]he ‘major peaks’ herein refer to peaks higher than the average of the peaks in the result.” (EX1001, 13:6–7.) But this lexicography argument fails.

To invoke lexicography, the alleged definition must be clear, deliberate, and unambiguous such that a person of ordinary skill in the art would readily understand the scope of the term. *MultiForm Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998). Moreover, even if the applicants meant to define the phrase, “major peaks,” there is still a question of what the phrase “peaks higher than the average of the peaks in the result” means to a POSA in the context of an alignment plot obtained by following the Ayres2008 method. And what Patent-Owner says this phrase means is *not* correct. See *Kumar v. Ovonic Battery Co., Inc.*, 351 F.3d 1364, 1368 (Fed. Cir. 2003). There, the Federal Circuit found the claim term “amorphous” was controlled by an explicit definition and meant “exhibit[ing] no long range order.” *Id.* Nevertheless, the Federal Circuit found that the words “no long range order” were unclear in the context of the invention and therefore remanded for further claim construction. *Id.* at 1372.

Patent Owner asserts that determining the “average of the peaks in the result” requires a specific multi-step numerical procedure that is not described in

the '223 patent, Ayres2008, or any other prior art reference. According to Patent-Owner, one must first identify all peaks in an FFT plot, assign numerical values to each peak, calculate an arithmetic mean of those values, and then designate as “major peaks” only those peaks exceeding that mean. (Paper-24, 7–8, 12–13.) Patent-Owner then argues that because Huang2 discloses only one peak in a 180-degree field, or two peaks of equal height in a 360-degree field, the average would equal the peak values themselves, such that neither peak would be higher than the average and thus neither would qualify as “major.” (*Id.*, 12–13.) On that basis, Patent Owner contends that Huang2 does not disclose “major peaks” within the meaning of claim 1 and therefore cannot invalidate the '223 patent. (*Id.*)

This argument is deeply flawed. Not only is Patent-Owner’s proposed numerical averaging approach nowhere disclosed in the specification, but it directly contradicts Ayres2008, which the '223 patent incorporates by reference as the authoritative guide for performing FFT analysis. It also contradicts the specification’s express teachings and the prosecution history.

(a) Patent-Owner’s Claim Construction is Inconsistent with the Specification and Ayres2008

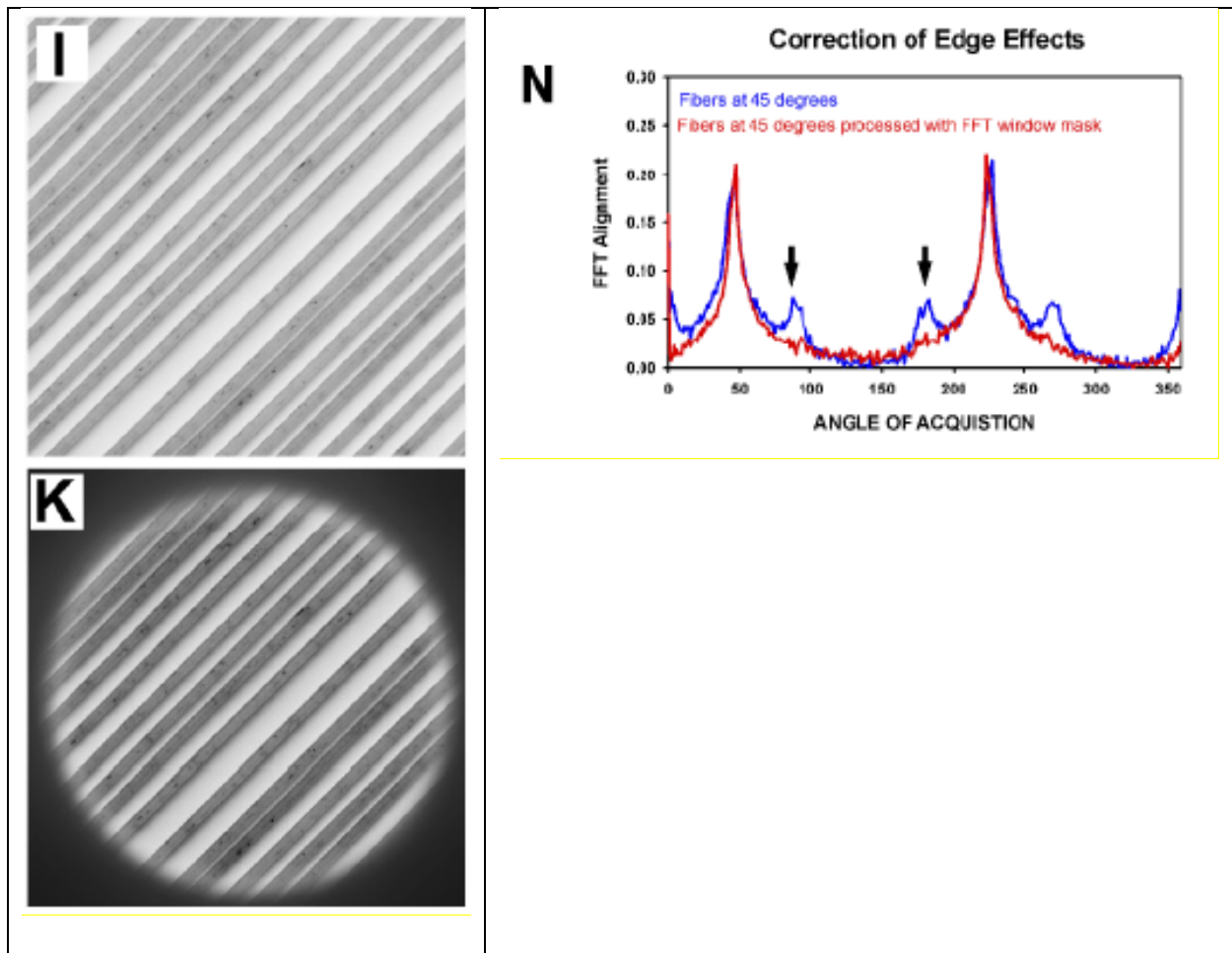
Neither the '223 patent nor Ayres2008 describes summing peak values, calculating an arithmetic mean, and using that mean to determine fiber alignment. (EX1220, 63:6–9, 86:3–5, 95:1–7; EX1219, ¶10.) If such a calculation were central to the claimed invention, the patent would necessarily describe how to perform it.

It does not. The '223 patent does not even label or numerically identify peaks in Figures 8A or 8B, the only FFT alignment plots disclosed. (EX1001; *see also* EX1220, 64:6–17.)

Instead, the '223 patent directs a POSA to Ayres2008, which it incorporates in its entirety. Ayres carries out a *visual assessment* of the relative sizes of the peaks to determine which peaks are “major” and thus indicate scaffold alignment. Ayres2008 explains that: “The 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). The 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.” (EX1010, 610 (emphasis added); *see also* EX1220, 76:7-12.) “The overall 2D FFT alignment value for a scaffold *is determined by visually inspecting and selecting* the maximal value from the peak of the alignment plot.” (EX1010, 613 (emphasis added).) This is how a POSA would understand the phrase “major peaks” in the context of the '223 patent and is the correct claim construction.

This understanding was confirmed by Dr. Simpson, the senior author of Ayres2008, who testified that identifying “major peaks” is a visual comparison of relative peak height and that references to an “average” reflect this qualitative assessment, not a numerical calculation. (EX2017, 88:6–89:9; EX1219, ¶¶5-10.)

Ayres2008 also provides concrete examples. In Figure 3, Ayres presents FFT plots of a highly aligned scaffold. The blue trace contains additional peaks caused by edge-effect noise (designated by arrows), while the red trace uses masking to eliminate artifacts and shows only two peaks, accurately reflecting complete alignment. (EX1010, 614–15.)



Both plots represent the same aligned fibers, but the red trace is more accurate precisely because it removes noise. Yet under Patent-Owner’s proposed construction, the exact same scaffold would fall outside the claims when plotted

with a mask that removes noise (red trace) but fall within them when plotted without a mask (blue trace). (EX1220, 83:21–84:23; EX1219, ¶¶12-16.) That result is nonsensical and contradicts the teachings of Ayres2008. (EX1219, ¶¶6-16); *see AstraZeneca AB v. Mylan Pharms. Inc.*, 19 F.4th 1325, 1329 (Fed. Cir. 2021)(selecting the claim construction that “‘most naturally aligns with the patent’s description of the invention,’ as further informed by the prosecution history”). The same is true of Huang2. Because the fibers in Huang2 are highly aligned, its FFT plot reflects only two major peaks 180 degrees apart when extended to 360 degrees. (EX1219, ¶17.)

Patent Owner’s claim construction effectively limits the claims to FFT plots that contain noise or imperfections. (EX1219, ¶11.) Indeed, Patent-Owner’s expert, Dr. Mikos, testified that his claim construction would necessarily require the presence of some misaligned fibers to generate additional peaks. (EX1220, 79:2–13, 80:6–16.) Nothing in the patent suggests that misalignment is required to practice the claimed invention. (EX1219, ¶12.)

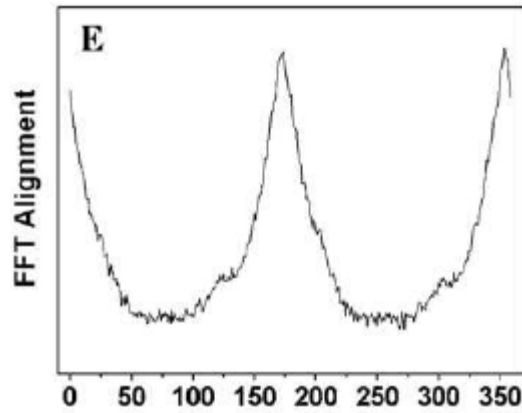
Indeed, Patent-Owner’s claim construction collapses when applied to the patent’s own examples. According to the specification, and as argued by Patent-Owner, Figure 8A shows aligned fibers within the scope of claim 1, but Figure 8B shows random fibers not within the scope of the claim. (Paper 24, 5; EX2015, ¶ 51; EX1001, 1:56–57.) Yet under Patent-Owner’s lexicographer argument, the FFT

plot for Figure 8B would fall within claim 1 because two of its four peaks exceed the calculated average and thus would be considered adjacent major peaks 180° apart. (EX1219, ¶¶18-19.) Patent-Owner’s expert, Dr. Mikos, also testified as to the height of the four peaks in figure 8B. (EX1220, 65:6-66:11, 69:2-23.) Taking the average—as Dr. Mikos asserts one must do—would mean that there are two peaks 180° apart that exceed the average and thus fall within the scope of the claims. Patent-Owner’s claim construction thus captures the patent’s control example, which cannot be correct. In contrast, Ayres2008’s visual test explains that four peaks of “nearly uniform height” indicate random fibers. (EX1010, 609.) Thus, under the Ayres2008 visual test, which is part of the patent specification, the random control sample would *not* fall within the scope of the claims, which is exactly what the specifications teaches, and is thus how a POSA would understand the claims. (EX2019, ¶19.)

(b) Patent-Owner’s Claim Construction is Contradicted by the Prosecution History

The prosecution history further confirms that Patent Owner did not understand “major peaks” to require any numerical averaging. “[A]ny explanation, elaboration, or qualification presented by the inventor during patent examination is relevant, for the role of claim construction is to ‘capture the scope of the actual invention’ that is disclosed, described, and patented.” *AstraZeneca*, 19 F.4th at 1335.

During prosecution, the Examiner rejected the claims in view of Huang1 (Fig. 4E), which discloses only two peaks at “175 degrees and 355 degrees (180 degrees apart)” in a scaffold with fibers made from pure TPU (EX1002, 211; EX1008, 309, Fig. 4E; EX1220:2-17.)¹



Patent Owner did not dispute that those peaks were “major.” Instead, Patent Owner amended the claims to require collagen. (EX1002, 238.) However, under Patent Owner’s current theory, Fig. 4E of Huang1 would disclose no major peaks at all, directly contradicting the Examiner’s rejection and Patent-Owner’s acquiescence.

(c) Patent-Owner’s Claim Construction Contradicts its Position at the District Court

Patent-Owner’s current numeric averaging contradicts its infringement position in district court, where it did not carry out its peak averaging calculation. Instead, Patent-Owner relied on statements that Embody’s products were “highly

¹ In an FFT, the peaks at 0° and 355° are the same. (EX1220, 62:16-20.)

aligned.” (EX2005, ¶¶49-52.) Patent Owner cannot adopt one claim construction to avoid invalidity while asserting another for infringement. *Paypal Holdings, Inc. v. Fintiv, Inc.*, IPR2023-00744, 2024 WL 4375951, at *8 (PTAB Oct. 2, 2024).

(d) Patent-Owner’s Claim Construction Relies on an Expert with No Applicable Experience with FFT

Patent Owner’s claim construction requiring calculation of a numerical mean rests entirely on the unsupported testimony of its expert, Dr. Mikos. Dr. Mikos admitted that he has never performed FFT testing himself and could not identify a single publication in which he used FFT analysis to generate an alignment plot as described in Ayres2008 and depicted in the ’223 patent. (EX1220, 32:8–20, 35:2–36:17, 52:8–20; EX1219, ¶24.) There is no evidence that Dr. Mikos has ever applied the Ayres2008 method in practice.

At deposition, the only paper Dr. Mikos identified was published in 2021, does not follow the Ayres2008 methodology, and does not include an alignment plot. (EX1203; EX1219, ¶19.) Thus, Patent Owner’s proposed numerical-mean requirement is not grounded in the patent, the cited prior art, or Dr. Mikos’s own experience.

By contrast, Petitioner’s expert, Dr. Simpson, is the author of the Ayres2008 paper expressly incorporated into the ’223 patent and has performed extensive FFT analyses using that method. Dr. Simpson testified that he has never used, nor understood the art to require, a numerical average calculation as a prerequisite to

identifying major FFT peaks or determining fiber alignment. (EX1219, ¶¶5-9.) His testimony reflects the understanding of a POSA and is firmly rooted in the intrinsic record.

Unable to rebut this evidence, Dr. Mikos attempts to redefine the person of ordinary skill in the art by asserting that an engineering degree is required. (EX2015, ¶39; EX1219, ¶25.) That assertion is unsupported and contrary to the field. Dr. Simpson holds a Ph.D. in cell biology and anatomy, as do many practitioners who routinely perform FFT-based alignment analyses. Dr. Mikos's proposed redefinition is a litigation-driven effort to discount authoritative testimony rather than a reflection of the relevant art. Accordingly, Patent Owner's expert-driven numerical-mean claim construction and its improper definition of a person of ordinary skill in the art should be rejected.

3. The Board Should Credit Dr. Simpson's Testing

(a) Dr. Simpson Established that Huang2 has Two Major Peaks as Set forth by Claim 1

Dr. Simpson, who is senior author of the Ayres2008 paper, tested the image set forth in Huang2 using his FFT analysis and confirmed that it has the two major peaks required by the claims, as would be understood by a POSA. (Paper-2, 31–33; Paper-14, 26–27; EX1219, ¶¶21-23.) Further, both the Petition (and Dr. Simpson's declaration) stated, as noted by the Board, that that the two peaks are “necessarily” there. (Paper-2, 22–23, 31; EX1003, ¶¶106, 109.) Accordingly, Dr. Simpson's

testing confirms that a POSA would understand that Huang² has the two major peaks recited in the claim.

(b) Patent-Owner's Criticisms of Dr. Simpson's Huang² Testing Are Meritless

In response, Patent Owner conducted no testing of its own and instead attempts to undermine Dr. Simpson's analysis by quibbling over minor details, effectively arguing that the inventor of the method does not know how to perform the method he himself developed. (See EX1219, ¶¶26-27.) Patent-Owner never explains how any of the alleged deficiencies in Dr. Simpson's analysis would alter the results, which alone defeats its arguments. Dr. Simpson, who invented and published the Ayres²⁰⁰⁸ method, should be credited over Dr. Mikos, who has never performed the Ayres²⁰⁰⁸ method or published a paper including an alignment plot.

Patent Owner's criticisms also lack merit. Patent Owner contends that Dr. Simpson's testing is invalid because he did not specify details such as illumination, noise, image type, software version, circular projection placement, or masking. (Paper-24, 26–29.) But Dr. Simpson explained that he performed the analysis in accordance with Ayres²⁰⁰⁸, which is precisely the level of detail provided in the '223 patent itself. (EX1001, 13:16–26; EX1219, ¶¶28.) As Patent Owner's expert admitted, none of the details Patent Owner now demands appear in the '223 patent. (EX1220, 116:2–12, 117:10–16, 118:1–10.) A POSA would thus readily know

how to carry out the Ayres2008 method, particularly its inventor. Well-established precedent forecloses Patent Owner's attempt to require more detail in the prior art than appears in the challenged patent. *See Uber Techs., Inc. v. X One, Inc.*, 957 F.3d 1334, 1339 (Fed. Cir. 2020); *In re Publicover*, 813 F. App'x 527, 532 (Fed. Cir. 2020); *Donghee Am., Inc. v. Plastic Omnium Advanced Innovation & Research*, IPR2017-01633, 2019 WL 80465, at *5 (PTAB Jan. 2, 2019)(finding obviousness where the patent owner did not provide in the specification the "the type of detail [it] now argues is necessary in the prior art references").

Dr. Simpson further addresses and rebuts Dr. Mikos's criticisms in a supplemental declaration. (EX1219, ¶¶ 29-39.) With respect to masking, Ayres2008 teaches the use of masking to reduce noise, and Dr. Simpson explained that a person of ordinary skill would understand when masking is appropriate. (EX2017, Tr. 208:18-209:18.) Dr. Simpson also performed FFT analyses both with and without masking, and both demonstrate the requisite peaks. (EX1219, ¶39.) As to image quality, Dr. Simpson testified that the Huang2 image is more than sufficient for FFT analysis, that FFT is a "pretty forgiving" technique, and that even imperfect images may be used. (EX2017, 61:11-15, 138:23-139:14.) He further explained that Biomaterials would not have published Huang2 without an image suitable for analysis. (*Id.*, 142:10-18.)

Dr. Simpson has also intentionally introduced noise into the Huang2 image and demonstrated that, even with significant noise, the FFT still produces the requisite two peaks. (EX1219, ¶35.) Patent-Owner's suggestion that FFT analysis may be performed only on "original" data would preclude FFT analysis of any published image, no matter how clear, and should be rejected.

(c) Dr. Simpson's Testing Is Consistent with and Confirms the Teachings of Huang2 to a POSA

Patent-Owner further argues that Dr. Simpson's testing should be disregarded because it is different from the FFT in Huang2 and thus unreliable. (Paper-24, 22-26.) Patent-Owner argued that "Dr. Simpson's testing depicts two minor peaks in the FFT plot, at 0° and 180°, that are absent and not disclosed by Huang2." (*Id.*, 14.) But, Ayres2008 states that the smaller peaks, like the ones in Dr. Simpson's FFT plot, generally correspond to "background noise." (EX1010, 615; EX 2017, 92:12-15, 118:13-119:5; EX1219, ¶40.) Notwithstanding the Patent-Owner's reliance on noise, both Dr. Simpson's FFT and the FFT in Huang2 disclose only one major peak in a 180° field. (EX1219, ¶40.) The two FFT plots are thus perfectly consistent. (EX1219, ¶40.) Patent-Owner itself acknowledges that the FFT plot in Huang2 may represent the average plot of separate FFT analysis run on five different images taken of different parts of the scaffold. (*See* Paper-24, 18-22; EX2015, ¶90; EX1220, 100:16-101:14.) In contrast, Dr. Simpson ran his FFT on the single image that was published in Huang2. (EX1219, ¶ 41.) This

difference explains why Huang2's FFT plot is not identical to that run by Dr. Simpson. (EX1219, ¶41.)

4. Dr. Simpson's Testing Meets Even Patent-Owner's Construction

The Federal Circuit has made clear that a petitioner may raise new arguments in response to a claim construction advanced for the first time by Patent Owner after institution. *Axonics, Inc. v. Medtronic, Inc.*, 75 F.4th 1374, 1380 (Fed. Cir. 2023). Petitioner is therefore entitled to address Patent-Owner's new claim construction introduced in its response. Notably, Patent Owner's own expert, Dr. Mikos, identified four peaks in Dr. Simpson's alignment plot during his deposition. (EX1220, 109:11–110:14.) Applying Dr. Mikos's proposed arithmetic mean calculation to those identified peaks yields two peaks above the average, which would be considered "major peaks." (EX1219, ¶ 42.) Because those two peaks are separated by 180°, they satisfy the claim limitations even under Patent Owner's erroneous construction. (*Id.*)

B. Huang2 Anticipates Dependent Claims 2-3, 5-12

For the dependent claims, Patent-Owner only raised additional patentability arguments for claims 2 and 3.

Claim 2 requires that the fibers comprise type 1 collagen in its native triple helical structure. The Petition explains that Huang2's use of type 1 collagen as a *starting material* meets this claim element. (Paper-2, 33–34.) Patent-Owner argues

the collagen is not in triple helical form *after* being electrospun. But the claim does not require that the collagen remains in its triple helical form after being electrospun. Indeed, the patent has *no teaching* related to maintaining the collagen in its native form, or reporting the structure of the collagen after electrospinning, and its only teaching related to collagen is including collagen in a list of possible *starting* materials. (See EX1001, 14:27-34; EX1219, ¶44; EX1220, 128:7-16.)

Regardless, Patent-Owner's technical arguments are incorrect. (EX1219, ¶¶45-49.) Patent Owner argues that the solvent used by Huang², HFIP, breaks down the collagen. (Paper-24, 30-31.) But the patent also uses HFIP (EX1001, 19:40-43), and 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*." (EX1209, 1205 (emphasis added); EX1220, 141:4-142:2; EX1219, ¶45.) Patent-Owner also argues that the acid by-products of PCL will break down the collagen (Paper-24, 30), but again, the patent teaches using blends of collagen and PCL, and Patent-Owner's own cited art demonstrates that PCL is stable for 3-4 years. (EX2018, Abstract.) While Dr. Mikos argues that degradation problem happens "during storage" (EX2015, ¶110), the claims do not require storage. (EX1219, ¶47.) Patent-Owner also argues that the fetal bovine serum ("FBS") in Huang² eliminates the triple helical collagen. (Paper-24, 30.) But FBS is used for cell

culture in Huang2, claim 2 does *not* require cell culture, and Huang2’s scaffold is made without the use of FBS. (EX1005, 1792 (2.2 nanofibrous matrix preparation).) The ’223 patent makes clear that a scaffold need not have cells cultured on it, which is a separate and “optional” embodiment of the alleged recited in claim 11. (EX1001, 1:23-30; IPR2025-00249, EX1002, 652-653; EX1219, ¶¶ 48-49.)

Claim 3 requires the scaffold to have less than 8% residual calcium by weight. Patent-Owner argues that the calcium content in Huang2’s scaffold could be greater than 8% by weight because the collagen could have been isolated using reagents comprising calcium. (Paper-24, 32.) This argument constitutes pure speculation and can be rejected on that basis alone. (See EX1219, ¶50.) Moreover, Patent-Owner’s arguments concerning the presence of calcium in FBS are misplaced, as set forth above. (See, *id.*)

C. Huang2 and Kumbar Render Claim 4 Obvious

Claim 4 requires an “average porosity from about 60% to about 90%,” a range that is obvious based on Huang2 in light of Kumbar. (EX1001, claim 4; see Paper-2, 55–56; Paper-14, 33-34.) In response, Patent-Owner’s main argument is that there would have been no expectation of success in obtaining this range in an aligned scaffold. (Paper-24, 36.) The ’223 patent itself, however, describes ranges of potential porosity values that range from a low of 60% to a high of 95%, and,

there is *no teaching* how to obtain such porosity in aligned fibers. (EX1001, 14:21-26; *see also* EX1219, ¶¶51-58.) This means a POSA would understand how to obtain such ranges based on the prior art. *See Uber Techn.*, 957 F.3d at 1339; *see also In re Publicover*, 813 F. App'x at 532; *Donghee Am.*, 2019 WL 80465, at *5.

Further, the prior art established that fiber size is the most important factor in obtaining a high porosity. (EX1214, 7; EX1220, 148:9-19; EX2017, 16-18.) And there are multiple publications, including by Dr. Mikos, where the authors adjusted fiber size by adjusting the parameters used for electrospinning. (*E.g.*, EX1006, 2; EX1215, 2800, Tables 1-2; EX1219, ¶54.) Consistent with these publications, the prior art showed scaffolds containing aligned fibers that have the claimed porosity. (EX1211, 7, Table 2 (aligned electrospun scaffold with 75.7% porosity); EX1212, 120-122, Figure 6 (aligned scaffolds with porosities ranging from 81-88%); EX1213, 1207, Table 1 (aligned scaffolds with porosities ranging from 74.85-78.57%; EX1219, ¶55.) Further, and contrary to Patent-Owner's assertions (Paper-24, 35), measuring porosity is a conventional routine process in the prior art, as established by Dr. Mikos's own papers. (*See* EX1215, 2800; EX1219, ¶57.)

D. Lee Anticipates Claims 1-12

1. Claim 1 is Anticipated

(a) Lee's Highly Aligned Fibers Have the Claimed Peaks

Contrary to Patent-Owner's assertions (*see* Paper-24 at 39–40), the Petition is not “unclear” but relies on 35 U.S.C. § 102 and argues that Lee anticipates each of the challenged claims. (Paper-2, 47.) In terms of the required FFT peaks, the Petition argues that Lee discloses this element to a POSA by disclosing aligned fibers, which by definition, must have two major peaks in the FFT 180° from each other. The Petition argues that “Lee discloses aligned PCL/collagen fibers that meet this element of the claim.” (Paper-2, 49 (citing EX1003, §VI.C.1.c).) EX1003 is the declaration of Dr. Simpson, who expands upon the point in this section, explaining that “an FFT analysis measures the degree of fiber alignment, and an FFT result showing fibers having adjacent major peaks with about 180° apart from each other *only occurs when the fibers are aligned.*” (*See* EX1003, §VI.C.1.c, ¶181 (emphasis added).) Indeed, as Patent Owner acknowledges in the Patent-Owner's Response, it was well-known in the prior art, as published by Ayres2008, which has been cited hundreds of times, that “scaffolds containing aligned elements exhibit . . . two larger peaks at 90° and 270°,” which are 180° apart. (EX1010, 610; EX1219, ¶¶59-60; Paper-24, 3-4 (citing EX1010, 610).) The Petition then goes through the extensive evidence demonstrating to a POSA that Lee obtained highly aligned collagen blended fibers, including fiber orientation testing using computer

analysis and mechanical testing (Paper-2, 49–52.) Dr. Simpson’s own testing further confirmed that the fibers are aligned. (*Id.*, 52–53.) And Patent-Owner does not challenge that Lee obtained highly aligned collagen blended fibers. (Paper-24, 59–60; EX2015, ¶190; EX1220, 192:6-15.)

This is sufficient to establish that Lee discloses the FFT element of the claims as highly aligned fibers must have the requisite two peaks in the FFT. (EX1010, 609.) In fact, as mentioned above, the Patent-Owner itself argued at the district court that “highly aligned” fibers fall within the scope of the claims. (EX2005, ¶¶49-52); *see Bristol-Myers Squibb Co. v. Ben Venue Lab'ys, Inc.*, 246 F.3d 1368, 1378 (Fed. Cir. 2001)(“that which would literally infringe if later anticipates if earlier.”)

Patent-Owner, however, argues that Dr. Simpson’s testing shows that the peaks are there inherently, which it argues was not raised. (Paper-24, 39–40.) Inherency, however, typically examines whether properties that are *unknown* and *not recognized* by a POSA in the prior art are nevertheless there. *Honeywell International Inc. v. Mexichem Amanco Holding SA DE CV*, 865 F.3d 1348, 1354 (Fed. Cir. 2017). As a POSA reading Lee *would have* known and understood that Lee’s highly aligned fibers have the necessary FFT peaks, Petitioner argued that Lee discloses to a POSA the required peaks by describing highly aligned fibers.

Moreover, the Petition specifically asserts inherency. 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).)

Thus, whether the Board finds that a POSA would understand that the requisite peaks are there because of the extensive testing performed in Lee to show alignment or that the peaks are “inherently” there, the result is the same. As the Board found in *AMCOL Int’l Corp. v. Oil-Dri Corp. of Am.*, IPR2022-01107, 2023 WL 8264190, at *9-10 (P.T.A.B. Nov. 29, 2023), “[w]e do not see the bright line distinction between Petitioner’s approach [what a POSA would “understand” from the prior art] and the inherency standard that Patent-Owner suggests because, as Petitioner asserts, the same evidence can satisfy both standards.” *Id.*

(b) Patent-Owner's Criticisms of Dr. Simpson's Lee Testing Lack Merit

Patent-Owner's criticisms of Dr. Simpson's testing are recycled from its arguments concerning Huang2, and Petitioner's response above apply equally here. (See §§II.A.3.(b), *supra.*; EX1219, ¶63) Patent-Owner's main challenge seems to be that the image quality that Dr. Simpson analyzed from Lee is too low. But 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. (EX1219, ¶¶63-64.) Further, if one uses the criteria Dr. Mikos has used to select what he designates as "peaks," Dr. Simpson's testing of the image set forth in Lee shows the requisite major peaks 180° apart, even under Patent-Owner's own flawed claim construction.

2. Lee Anticipates Dependent Claims 2-12

Patent-Owner only offers additional arguments concerning dependent claims 2, 3, 4, and 12. Patent-Owner's arguments concerning claims 2 and 3 are the same as with regard to Huang2 and fail as previously discussed. (See § II.B., *supra.*)

For claim 4, the Petition explains that Lee discloses that, in some embodiments, its electrospun nanofiber scaffolds have high porosity, and incorporates Mikos in its entirety, which discloses that high porosity is greater than 80% by volume. (Paper 2, 55-56; EX1219, ¶66.) This plainly falls within the claimed range of 60% to 90%, which contrary to Patent-Owner's assertions, is

more than sufficient for anticipation. *See Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1338 (Fed. Cir. 2020). Further, as discussed above, the '223 patent is silent concerning how to achieve the claimed porosity, relying on the skill of a POSA to achieve the claimed range. This refutes Patent-Owner's assertions that a POSA could not achieve the claimed porosity based on the prior art. (EX1219, ¶67.)

Claim 12 requires a method of culturing cells on the scaffold, where the cells may be "stem cells." Lee teaches culturing "skeletal muscle cells" on its scaffold and explains that skeletal muscle cells include "myoblasts." (EX1011, [0007], [0040].) Lee further teaches that "myoblasts are a type of muscle stem cell." (Lee, [0030]; Paper-2, 64; *see also* EX1217, 455.) Patent-Owner's assertions to the contrary (Paper-24, 57-58) are wrong. (EX1219, ¶68.)

E. Lee Renders Claims 1-12 Obvious

While the Board on institution indicated that the above discussion should resolve Lee (Paper-14, 38–39), the Petition also expressly argued a POSA "would have been motivated" to use FFT to confirm that orientation of the fibers and would have a reasonable expectation of success in doing so. (Paper-2, 65).

Patent-Owner argues that there would have been no motivation to run an FFT on Lee's fibers because Lee already confirmed that the fibers are highly aligned. (Paper-24, 59–61.) But Patent-Owner ignores that the techniques used in

Lee (analysis of an SEM image and mechanical testing) are *destructive* of the scaffold just created. (EX1220, 54:5-8, 56:13-57:9; EX1219, ¶¶ 69-71.) The FFT technique invented by Dr. Simpson is *non-destructive*. (EX1003, ¶11; EX1220, 55:5-17.) Thus, if a POSA wanted to follow the techniques of Lee to engineer a scaffold that could be used to treat a tissue injury, and wanted to confirm fiber alignment, the POSA would use FFT as it is a simple, non-destructive technique, that can be used on a brightfield microscope image of the scaffold, and the scaffold can be subsequently used to treat the injury. (EX1010, 620; EX1219, ¶71.) Patent-Owner's statements to the contrary are wrong.

III. CONCLUSION

Petitioners respectfully submit that the challenged claims are unpatentable.

Respectfully submitted,

Dated: February 4, 2026

By: /Howard W. Levine/
Howard W. Levine (Reg. No. 41,453)

IV. CERTIFICATE OF COMPLIANCE

The undersigned hereby certifies that the foregoing **Reply to Patent-Owner's Response** contains 5360 words, as measured by the word-processing system used to prepare this paper.

Dated: February 4, 2026

By: /Howard Levine/
Howard Levine (Reg. No. 41,453)

CERTIFICATE OF SERVICE

I hereby certify that on February 4, 2026, I caused a true and correct copy of the forgoing Reply to Patent-Owner's Response to be served via electronic upon to the Patent-Owner's counsel of record at the following addresses:

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