

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AXION BIOSYSTEMS, INC.,
Petitioner

v.

AGILENT TECHNOLOGIES, INC.,
Patent Owner.

Case IPR2024-01467

U.S. Patent No. 11,906,508

**PETITIONER REPLY TO
PATENT OWNER RESPONSE**

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UPDATED LIST OF PETITIONER EXHIBITS

EX1001	U.S. Patent No. 11,906,508 (the “508 patent”)
EX1002	File History for U.S. Patent No. 11,906,508
EX1003	Declaration of Dr. Bruce Kim
EX1004	Curriculum Vitae of Dr. Bruce Kim
EX1005	U.S. Patent No. 7,192,752 to Xu et al. (“Xu-752”)
EX1006	U.S. Patent Application Publication No. 2007/0057680 to Jones et al. (“Jones”)
EX1007	U.S. Patent No. 7,459,918 to Jones et al.
EX1008	“Real-Time Monitoring of Morphological Changes in Living Cells by Electronic Cell Sensor Arrays: An Approach To Study G Protein-Coupled Receptors,” by Naichen Yu et al., <i>Analytical Chemistry</i> , Vol. 78, No. 1, 35-43 (January 2006) (“Yu”)
EX1009	Reserved
EX1010	Scheduling Order in <i>Agilent Technologies, Inc. v. Axion BioSystems, Inc.</i> , Case No. 1:24-cv-300-CJB (D. Del.) (D.I. 24, dated June 21, 2024)
EX1011	Reserved
EX1012	PDF of Agilent’s Technology Tutorial for Xu-752 and related patents in <i>Agilent Technologies, Inc. v. Axion BioSystems, Inc.</i> , Case No. 1:23-cv-198-CJB (D. Del.) (D.I. 127) (April 5, 2024)
EX1013	U.S. Patent No. 9,709,548 to Wang et al. (“Wang-548”)
EX1014	File History Excerpts for Wang-548 (U.S.P.N. 9,709,548)
EX1015	U.S. Patent No. 7,459,303 to Wang et al. (“Wang-303”)
EX1016	U.S. Patent No. 7,470,533 to Xu et al. (“Xu-533”)

- EX1017 “Monitoring electroporabilization in the plasma membrane of adherent mammalian cells,” by Paramita M. Ghosh et al., *Biophysical Journal*, Vol. 64(5), 1602-1609 (May 1993) (“Ghosh”)
- EX1018 “Performance of a thin film microelectrode array for monitoring electrogenic cells in vitro,” by A. Mohr et al., *Sensors and Actuators*, B 34, 265-269 (1996) (“Mohr”)
- EX1019 “Portable cell-based biosensor system for toxin detection,” by Joseph J. Pancrazio et al., *Sensors and Actuators*, B 53, 179-185 (1998) (“Pancrazio”)
- EX1020 Reserved
- EX1021 “CMOS microelectrode array for the monitoring of electrogenic cells,” by F. Heer et al., *Biosensors and Bioelectronics* 20, 358-366 (March 2004) (“Heer”)
- EX1022 “A novel microfluidic impedance assay for monitoring endothelin-induced cardiomyocyte hypertrophy,” by Mo Yang et al., *Biosensors and Bioelectronics* (2006) (“Yang”)
- EX1023 “Real Time Monitoring Primary Cardiomyocyte Adhesion Based on Electrochemical Impedance Spectroscopy and Electrical Cell-Substrate Impedance Sensing,” by Yiling Qiu et al., *Analytical Chemistry*, Vol. 80, No. 4, 990-996 (February 2008) (“Qiu”)
- EX1024 Operating Manual for Solartron Analytical 1260 Impedance/Gain-Phase Analyzer (January 1996)
- EX1025 “Monitoring fibroblast behavior in tissue culture with an applied electric field,” by Ivar Giaever et al., *Proc. Natl. Acad. Sci. (USA)*, Vol. 81, 3761-3764 (June 1984) (“Giaever-1984”)
- EX1026 “A new planar multielectrode array for extracellular recording: application to hippocampal acute slice,” by Hiroaki Oka et al., *Journal of Neuroscience Methods*, Vol. 93(1), 61-67 (October 1999) (“Oka”)
- EX1027 Librarian Declaration
- EX1028 Dr. Benjamin Sanchez Terrones Deposition Transcript (Aug. 8, 2025)

I. INTRODUCTION

In disclaiming claims 16-22 following the Institution Decision, Agilent concedes that the hardware system of the '508 patent would have been obvious over the Xu-752/Jones combination. The only remaining dispute—whether a POSA would have used that system for monitoring impedances of two or more wells at a millisecond time resolution—is narrow and should be resolved in Axion's favor.

First, the Xu-752/Jones system is capable of millisecond time resolution measurements. Agilent focuses solely on one embodiment of Jones disclosing a 1.5 second update period when using a 96-well plate, but Agilent ignores what Jones explicitly discloses regarding its flexibility and other configurations that are capable of achieving millisecond time resolution. The '508 patent's claims are broad—they encompass the measurement of as few as *two wells* using a *single measurement frequency*. A POSA would have known that if Jones can achieve a resolution of 1.5 seconds in measuring *96 wells* via a *multi-frequency sweep*, then Jones was capable of measuring *two wells* at a *single frequency* (as described in Jones's ¶[0003]) with “millisecond time resolution.”

Second, a POSA would have been motivated to apply configurations of the Xu-752/Jones system capable of achieving millisecond time resolution measurements. The Petition cited documentary, prior-art evidence showing

applications of impedance-based cell monitoring requiring millisecond time resolution measurements. To apply the Xu-752/Jones system to such known applications, a POSA would have readily understood that the system must be configured to achieve a millisecond time resolution. Accordingly, the Petition's obviousness showing is not based on hindsight but rather documentary evidence and a POSA's knowledge at the time of the alleged invention.

Claims 1-8 and 11-15 should be canceled.

II. CLAIMS 1-8 AND 11-15 WOULD HAVE BEEN OBVIOUS IN VIEW OF XU-752 AND JONES.

A. Jones's Impedance Analyzer With Parallel ADCs Is Capable Of Millisecond-Time Resolution.

Agilent argues that Jones's impedance analyzer is not capable of millisecond-time resolution measurements, and therefore the Xu-752/Jones combination is allegedly missing the "millisecond time resolution" limitation of claims 1-8 and 11-15. Agilent is wrong.

1. Agilent Fails To Consider Jones For Everything It Teaches And Suggests.

Agilent argues that "Jones *only* discloses a time of 1.5 seconds between consecutive measurements of all the wells being evaluated," which is not "millisecond time resolution," as claimed. POR, 11-12, 22-23.¹ This is incorrect.

¹ All emphasis is added herein unless otherwise noted.

Jones's ¶[0030] describes one specific embodiment with a 1.5 second update period—*i.e.*, one using a multiple-frequency sweep and eight daughter boards for measuring “a 96 well plate with 12 wells per row plus four reference network channels,” EX1006, ¶¶[0012], [0018], [0030]—but Jones also describes other configurations that would have a faster update period. Jones explicitly discloses, *e.g.*, that its impedance analyzer can use (i) measurements at a single frequency instead of a multi-frequency stepped sweep, (ii) three reference channels instead of four, and (iii) one daughter board per column instead of one per row (providing 12 daughter boards instead of eight, in a system accepting 96-well plates):

The system can be used for impedance measurements of varying time periods, ***single or multiple frequencies***, and various measurement rates.

Id., ¶[0003].

In an additional embodiment, ***each column of sensors, rather than each row of sensors, on a microtiter plate is addressed by measurement circuitry on a single daughter board*** with the system arrangement of the boards remaining the same.

Id., ¶[0025].

For in-run compensation, three precision RC networks are included in the system. In one embodiment, three precision RC networks are included. An alternative embodiment includes four reference networks. Additional embodiments may include any number greater than three.

Id., ¶[0042].

Jones also references “various measurement rates,” and the 96-well plate referenced in Jones's ¶[0030] is not required; Jones states that its system can

measure impedance for “a single well or multiwell microtiter plate.” *Id.*, ¶[0003], Abstract.

Agilent’s selective reading of Jones ignores these disclosures, violating the principle that a reference must be considered for everything it teaches. *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1076 (Fed. Cir. 2015). Jones’s ¶[0030] describes a single embodiment (“For an *embodiment* in which a 96 well plate”), and Agilent errs in failing to consider the alternative configurations that Jones discloses or suggests to a POSA. *Bradium Techs. LLC v. Iancu*, 923 F.3d 1032, 1049 (Fed. Cir. 2019) (A reference must be considered “not only for what it expressly teaches, but also for what it fairly suggests” to a POSA.) (quotation omitted).

2. The POR Concedes That Configurations Described In Jones Would Have A Millisecond Time Resolution.

Axion’s expert Dr. Kim explained that Jones discloses other configurations with an update period faster than 1.5 seconds. For example, citing to Jones ¶[0003], Dr. Kim explained that “[t]he measurement rate for a single-frequency sampling (rather than a stepped sweep) in Jones for the entire 96-well plate would be significantly less than 1.5 seconds.” EX1003, ¶75. Importantly, Dr. Kim’s testimony about these configurations is uncontested, and Agilent elected not to even depose him.

Dr. Kim also explained that using twelve daughter boards (*i.e.*, using “one daughter board for each column, rather than each row, of wells,” as described in

Jones ¶[0025]) would “lower[] the time needed to measure impedance in each well when compared to the configuration using only eight daughter boards.” EX1003, ¶74. Dr. Kim further testified that in measuring a “multiwell plate having fewer wells [than 96]”—like the 16-well plate of Xu-752 (*e.g.*, EX1005, Fig. 2)—Jones’s impedance analyzer would “provid[e] a higher measurement rate with less time between two measurements in each well.” EX1003, ¶75. And Dr. Kim’s calculations show that using three reference channels instead of four, as described in Jones ¶[0042], would result in a measurement rate of less than 1.5 seconds. *See* EX1003, ¶¶70, 137, 139.

Agilent does not contest any of these points, nor could it. Moreover, Agilent does not contest that the specific configurations of the Xu-752/Jones system detailed in Dr. Kim’s declaration (EX1003, as cited in the table below) would provide measurements satisfying all of the claimed millisecond time resolutions, *i.e.*, less than 500², 100, 40, 20, and 5 milliseconds, respectively, for claims 1 and 11-14. Dr. Kim’s examples apply different configurations of Jones’s impedance

² As explained in the Petition (at 13-14) and in Section III below, there are indefiniteness issues with “millisecond time resolution” in claim 1. For purposes of this proceeding, Axion adopts the POR’s position (at 12-15) that claim 1’s “millisecond time resolution” includes up to 500 milliseconds. The claims would also be unpatentable under a narrower “less than 300 milliseconds” construction, as shown in the Petition (at 36-47, 53-55, 63-65).

analyzer to the preferred 16- and 96-well plates of Xu-752 (*see, e.g.*, EX1005, Figs. 2, 3A):

EX1003	Number of Wells	Number of Frequencies	Daughter Boards	Reference Channels	Update Period
¶72	96-well	Single freq. (10, 50, or 100 kHz)	8	4	412-433 ms
¶137	16-well	Multi-freq. sweep	8	3	470 ms
¶139	16-well	Single freq. (10 kHz)	8	3	136 ms
¶173	16-well	Single freq. (10 kHz)	16	0	1.5 ms
¶175	16-well	Single freq. (10 kHz)	2	0	55 ms

Agilent does not address Dr. Kim’s examples, all of which show Jones’s capability for achieving a millisecond time resolution, including the fastest required by the challenged claims (*i.e.*, “less than 5 milliseconds” in claim 14).

Having failed to challenge these examples showing Jones’s capability of providing millisecond time resolution measurements, Agilent has waived any contrary arguments. Paper 10 (Scheduling Order), 9; *see also Google LLC v. DDC Tech., LLC*, IPR2023-00709, Paper 76 at 14-15, 58 (PTAB Nov. 4, 2024).

In sum, the embodiment of Jones’s ¶[0030] is just that—one embodiment.³ Jones discloses other configurations with the capability for millisecond time resolution measurements.

3. Jones’s Capability For Millisecond Time Resolution Measurements Is Well Within The Breadth Of Claim 1.

The breadth of claim 1 further shows why Agilent’s argument fails. *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 962-63 (Fed. Cir. 2014) (A POSA “need only have a reasonable expectation of success of developing the *claimed invention*.”) (original emphasis) (internal quotation omitted).

First, claims 1-8 and 11-15 encompass an impedance analyzer that takes impedance measurements at a single frequency. EX1028, 81:20-82:4; EX1001, claim 1. Jones likewise describes its system as being “used for impedance measurements of ... single or multiple frequencies” (EX1006, ¶[0030]), as does Xu-752 (EX1005, 12:43-13:33). While Jones does not explicitly state the number of frequencies for its “stepped sweep” (Jones ¶[0030]),⁴ any reduction (*e.g.*, from multiple frequencies to a single frequency) would yield a faster time resolution.

³ Agilent’s Exs. 2011-2013, indicating 2-10 second update periods for a 96-well plate in MDS Sciex’s commercial product, are beside the point. As discussed, Agilent has ignored Jones’s disclosures showing that Jones is also capable of faster update periods, including in the claimed millisecond ranges.

⁴ Dr. Sanchez testified that he has performed stepped frequency-sweep measurements using 3, 6, and 10 frequencies. EX1028, 89:15-25.

Here, Jones’s “stepped sweep” takes 68.2 milliseconds, while measurement at a single frequency (as Jones also discloses) would take significantly less time.

EX1003, ¶75.

Second, Jones ¶[0030]’s 1.5 second update period is when measuring a “**96 well plate** with 12 wells per row plus four reference network channels.” EX1006, ¶[0030]. But the ’508 patent’s claim 1 encompasses plates with a “plurality of wells” and thus the measurement of *as few as two wells*. EX1001, claim 1, 23:15-23; Pet., 11 (citing same); EX1028, 75:8-17. Jones likewise describes taking measurements of a “single well or multiwell microtiter plate” (EX1006, ¶[0003]), and Xu-752 discloses multiwell devices with as few as two wells (EX1005, 21:43-47). Measuring two wells—instead of 96—would further drive down Jones ¶[0030]’s 1.5 second update period.

Third, claim 1 encompasses both serial and parallel measurements. While Agilent’s suggestion that Jones’s parallel daughter boards are used one at a time lacks merit,⁵ claim 1 does not require that multiple wells be measured in parallel, in any case.

In sum, the ’508 patent’s claims include an apparatus capable of monitoring impedance for two (or more) wells, where the time between two consecutive

⁵ Agilent’s erroneous argument is rebutted in Section II.C below.

measurements for the wells is within the claimed millisecond time resolutions.

Jones discloses exactly such a system.

Scope of Claim 1	Jones
“plurality of wells” (<i>i.e.</i> , at least two)	“The present technology provides an Impedance Measurement System (ZMS) for measuring the complex impedance of each well of a <i>single well or multiwell microtiter plate.</i> ” EX1006, ¶[0003]; <i>see also id.</i> , Abstract.
measurements at a single frequency or multiple frequencies	“The system can be used for impedance measurements of varying time periods, <i>single or multiple frequencies</i> , and various measurement rates.” <i>Id.</i> , ¶[0003].
serial or parallel measurements	“Additionally, the ZMS <i>employs parallelism to obtain the required throughput</i> ” <i>Id.</i>

Ultimately, the ’508 patent does little more than describe the goal of millisecond time resolution; it provides no specific architecture for achieving that speed. Pet., 13. In contrast, Jones discloses significant engineering details, *e.g.*, daughter-board counts, reference channels, per-well measurement speed for an embodiment, etc. And what the ’508 patent does disclose—use of parallel ADCs and basic details, like the use of two or more wells, single- or multiple-frequency measurements, etc.—is taught by Jones. Agilent’s argument that the ’508 patent somehow enables millisecond time resolution measurements while Jones does not is unsupportable.

B. A POSA Would Have Been Motivated To Configure The Xu-752/Jones System For Millisecond Time Resolution Measurements.

At institution, the Board stated that “Dr. Kim’s examples modify multiple aspects of Jones’s 96-well embodiment,” but “Petitioner and Dr. Kim’s reasoning for those changes is [allegedly] not explained sufficiently in the Petition.” DI, 23-24. Axion respectfully disagrees. Dr. Kim’s examples apply configurations expressly disclosed in Jones to Xu-752’s preferred 16- and 96-well plates, and Dr. Kim’s reasoning is fully explained and not based on hindsight, as detailed below.

1. Dr. Kim’s Examples Do Not Rely On Hindsight.

Dr. Kim’s examples “are not based on hindsight reconstruction; rather, they are straightforward and logical and based on ... prior art” documentary evidence and a POSA’s knowledge at the time of the alleged invention. *PPC Broadband, Inc. v. Times Fiber Comms., Inc.*, IPR2022-01088, Paper 42 at 86 (PTAB Dec. 20, 2023). For example:

[1] There were applications of impedance-based cell analysis known to a POSA at the time of the ’508 patent that required millisecond-time resolution between measurements (*e.g.*, studying electroporabilization, where cell pores “start resealing within a few milliseconds,” EX1017 (Ghosh), 1604, 1609), and also specific cell behaviors that were known to a POSA to occur in milliseconds. Pet., 31-47; EX1003, ¶¶107-126; EX1008; EX1018-EX1023.

[2] A POSA understood that the biological cell phenomenon to be studied dictates the requisite measurement speed, and such speed must be commensurate with the cell dynamics being studied. Pet., 31-47, 63-65; EX1003, ¶¶107-126, 168-182.

[3] Accordingly, a POSA seeking to employ the Xu-752/Jones system to study electroporabilization or other known phenomena occurring at a millisecond time scale would have used the configurations expressly disclosed in Jones to achieve a measurement resolution adequate to measure the biological phenomenon at issue. Pet., 31-47, 63-65; EX1003, ¶¶107-126, 168-182.

As explained below, Dr. Kim’s analysis “takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made and does not include knowledge gleaned only from [the ’508 patent].” *In re McLaughlin*, 443 F.2d 1392, 1395 (CCPA 1971).

(a) Ghosh And Other Documentary Evidence Show Known Applications Of Impedance-Based Cell Analysis Requiring Millisecond Time Resolution.

The Petition (at 31-47) showed that there were “[s]everal ... applications” of “impedance-based cell-analysis systems” “known to a POSA at the time of the ’508 patent that used millisecond-time resolution between measurements.” Agilent concedes this point, failing to make any counter-arguments. Agilent does not contest, *e.g.*, that Ghosh describes the use of impedance-based cell analysis for studying electroporabilization, where cell pores “start resealing within a few milliseconds.” EX1017, 1604, 1609; EX1003, ¶178.

In fact, Agilent’s Dr. Sanchez did not even review Ghosh,⁶ and Ghosh refutes his opinion that “the ’508 Patent was the first to describe an impedance-

⁶ Dr. Sanchez—who replaced Agilent’s previous declarant Dr. Cunningham—did not consider key evidence supporting the combination of Xu-752 and Jones.

based cellular analysis with ‘millisecond time resolution’” (EX2009, ¶25). Fifteen years before the ’508 patent’s alleged priority date, Ghosh described “monitor[ing] the impedance of [a] sample” by “tak[ing] data once every 10 milliseconds” and noting the capability to “take readings as fast as once every 5 milliseconds.” EX1017, 1604, 1609. Ghosh thus described impedance-based cellular analysis with millisecond time resolution measurements, contrary to Dr. Sanchez’s unsubstantiated opinion.⁷ The ’508 patent’s alleged invention (measuring *two or more wells* at a millisecond time resolution) is, at most, a minor variation on Ghosh (measuring *a single sample* at a millisecond time resolution), and would have been obvious for all of the reasons stated in the Petition.

Aside from Ghosh, the Petition cited several other pieces of prior-art documentary evidence—EX1008 (Yu), EX1018 (Mohr), EX1019 (Pancrazio),

EX1028, 11:20-22, 18:15-18, 36:11-16; EX2009, ¶15. Dr. Sanchez’s understanding of obviousness is that “[i]t means combining two different patents ... renders [another] patent invalid because it was obvious to combine these two things together to achieve [what is claimed in the other patent].” EX1028, 14:8-18. Because Dr. Sanchez did not consider the evidence Axion cited for the Xu-752/Jones combination, he could not meaningfully assess obviousness, even under his own rudimentary understanding of it.

⁷ Dr. Sanchez “was still an undergrad” as of the ’508 patent’s May 2008 purported priority date, and he did not publish his first peer-reviewed article until 2011. EX1028, 28:22-29:20. To the extent Dr. Sanchez qualified as a POSA as of May 2008 (which Axion does not concede), he did so only barely. EX2009, ¶19 (agreeing with POSA definition requiring a B.S. degree plus at least 2 years of relevant experience or equivalent study).

EX1021 (Heer), EX1022 (Yang), EX1023 (Qiu)—showing that “there were applications of impedance-based cell analysis known to a POSA at the time of the ’508 patent that used millisecond-time resolution between measurements, and further there were also specific cell behaviors (*e.g.*, cardiomyocyte beating activity) that were known to a POSA to occur in short time periods (*e.g.*, milliseconds), such that millisecond-time resolution for measurements would be necessary and/or advantageous for any cell analysis system used to monitor such behaviors.” Pet., 41. Agilent did not address this evidence, or Axion’s showings based thereon, at all.

(b) A POSA Understood That The Cellular Phenomenon To Be Monitored Dictates The Requisite Measurement Speed.

The Petition (at 31-47, 63-65) showed that the biological cell phenomenon to be studied dictates the requisite measurement speed. Agilent does not argue otherwise, and Ghosh itself (as just discussed) makes this clear. *See* EX1017, 1604, 1609. Agilent’s Dr. Sanchez confirmed that the requisite measurement resolution is “driven by the application.” EX1028, 52:18-53:12. As he testified, “the problem in trying to measure things that have a dynamic component requires that the measurement needs to be fast enough to monitor that cellular activity, and if it is too slow a [POSA] would have understood that variation ... would look like [noise].” *Id.*

(c) A POSA Understood How To Configure The Xu-752/Jones System For Achieving Millisecond Time Resolution Measurements.

In view of the known applications requiring millisecond timescale measurements and a POSA's understanding that the measurement speed must match the dynamics of the cell behavior under study, Dr. Kim explained a POSA's understanding of how the configurations described in Jones would be applied to achieve the requisite millisecond time resolution measurements. As explained in Section II.A.2 above, for instance, Dr. Kim explained a POSA's understanding that applying a single measurement frequency (as disclosed in Jones ¶[0003]) rather than a stepped sweep would enable measurements at a faster resolution. EX1003, ¶75. Dr. Kim also explained a POSA's understanding of how Jones's reference channels would be adjusted for faster measurement times. *Id.*, ¶¶171-173 (explaining a POSA's understanding that unnecessary measuring of reference network channels would be eliminated, "e.g., because temperature and other drift factors do not change appreciably on a millisecond time scale").

* * *

In sum, the "relationship ... between" the prior-art applications "where faster sampling times are desirable" and Dr. Kim's examples (DI, 24) is evident: A POSA would have understood that to apply the Xu-752/Jones system for these prior-art applications, parameters such as those used in Dr. Kim's examples—all of

which are expressly disclosed in Jones—would be required. The Xu-752/Jones system thus renders obvious all of the claimed millisecond time resolutions—*i.e.*, less than 500, 100, 40, 20, and 5 milliseconds in claims 1 and 11-14.

2. The Petition Did Not Need To Address Purported Drawbacks Of The Proposed Combination, And Agilent Identifies No Such Drawbacks.

The Board stated that the Petition did not “account for any negative effects [the alleged] modifications (i.e., fewer wells, reference channels, frequencies, etc.) would have on Jones’s 96-well embodiment.” DI, 24 (citing *Arctic Cat Inc. v. Polaris Indus., Inc.*, 795 F. App’x 827, 833 (Fed. Cir. 2019)). Respectfully, the Petition was not required to address alleged drawbacks of its proposed obviousness combination, as the Board has recognized.

In *Life Spine, Inc. v. Globus Med., Inc.*, the patent owner argued that the petitioner’s obviousness theory failed because “[i]n determining whether a proposed modification would have been obvious, Petitioner was required to compare the benefits and drawbacks of the modification, but did not do so.” IPR2022-01435, Paper 36 at 95 (PTAB Apr. 18, 2024) (citing *Arctic Cat*, 795 F. App’x at 833) (internal citation omitted). The Board panel rejected this argument because it “mischaracterize[d] *Arctic Cat*”:

That case indicates that it is the “**Board** [who] must weigh the benefits and drawbacks of the modification against each other.” *Arctic Cat Inc.*, 795 F. App’x at 833 (emphasis added). Patent Owner points us to no case law indicating that Petitioner must anticipate and preemptively

address (in the Petition) alleged drawbacks Patent Owner might later raise at trial in the *inter partes* review.

Id. at 96 (emphasis in original). The *Life Spine* decision thus recognized petitioners asserting obviousness must “make a *prima facie* case of unpatentability” (*id.* at 96 n.22), but the petition need not identify supposed drawbacks of a proposed obviousness combination. No precedent requires a patent challenger to affirmatively identify “negative effects” in its obviousness argument.

Here, the Petition established the obviousness of claims 1-8 and 11-15. The Petition showed, among other things, a POSA’s “reason[s] to combine the known elements [of Xu-752 and Jones] in the fashion claimed by the [’508 patent],” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007), and reasons to configure the resulting system for millisecond time resolution measurements. Pet., 31-47, 63-65; EX1003, ¶¶107-126, 168-182. The Petition further showed a POSA’s reasonable expectation of success in achieving the proposed combination. Pet., 44-45, 65; EX1003, ¶¶122-123, 179.

Agilent has now had the opportunity to identify supposed drawbacks of the obviousness combination, but the POR identified **none**. The record thus contains no evidence of any “negative effects” (DI, 24) of the Xu-752/Jones system.

In any event, “a given course of action often has simultaneous advantages and disadvantages, and this does not necessarily obviate motivation to combine.” *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006). In *KSR*, for

instance, “evidence indicating that a prior-art product was ‘bulky, complex, and expensive’ wasn’t on its own enough to dismiss it as ‘too flawed to upgrade.’” *Intel Corp. v. Qualcomm, Inc.*, 21 F.4th 784, 795 (Fed. Cir. 2021) (quoting *KSR*, 550 U.S. at 425-26). And it is “not necessary to show that an [obviousness] combination is ‘the *best* option, only that it be a *suitable* option.’” *Intel*, 21 F.4th at 800 (emphasis in original) (citation omitted). The configurations the Petition describes would have advantageously enabled a POSA to study electroporabilization and other known cellular phenomenon at a millisecond time resolution. Pet., 31-47, 63-65. Even assuming the applied configurations are not “the best option[s]” for some applications—and no evidence in the record indicates as much—this does not obviate a POSA’s motivation for applying these configurations for the reasons stated in the Petition.

3. Agilent’s POR Arguments Fail.

First, Agilent argues that “a POSA would not look to Jones because Jones does not teach an impedance system capable of millisecond time resolution” (POR, 3), but this is wrong for the reasons explained above in Section II.A.

Second, Agilent argues that Jones does not “disclose or suggest improving the speed of making impedance measurements” (POR, 3), but this a strawman because the Petition did not rely on Jones’s disclosure as motivating the desire for faster measurements. As summarized in Section II.B.1 above, the Petition (at 31-

47, 63-65) provided numerous reasons why a POSA would have been motivated to achieve millisecond time resolution in the Xu-752/Jones system, but did not rely on Jones itself for the motivation.

Third, Agilent argues that “Jones does not mention any particular applications for its system, including the types of cells to be monitored.” POR, 26. This does not help Agilent. Instead, it confirms the broad scope of Jones’s disclosure and its applicability to a variety of different cell types, not only those for which a 1.5 second update period would have been sufficient.

Finally, Agilent argues that the purpose of Jones is to achieve temperature control in a system having a compact form factor, not to achieve faster measurements. POR, 3-7. But Agilent’s characterization of Jones is unduly narrow and inconsistent with Jones’s “broader teachings.” *Recor Med., Inc. v. Medtronic Ireland Mfg. Unlimited Co.*, No. 23-2251, 2025 WL 944511, at *3 (Fed. Cir. Mar. 27, 2025). Moreover, the Supreme Court rejected the notion that prior art is only relevant if it shares the same primary purpose as the challenged patent:

Common sense teaches ... that familiar items may have obvious uses beyond their primary purposes The idea that a designer hoping to make an adjustable electronic pedal would ignore Asano because Asano was designed to solve [a different problem than the challenged patent] makes little sense. A [POSA] is also a person of ordinary creativity, not an automaton.

KSR, 550 U.S. at 420-21; *see also In re Heck*, 699 F.2d 1331, 1332-33 (Fed. Cir. 1983).

Here, likewise, a POSA would not have ignored Jones because it allegedly has an “express focus on a compact form factor and temperature control in conjunction with closely packed parallel daughter boards.” POR, 6-7. The Petition explained that “parallel processing of data streams [as described in Jones] was a well-known technique to improve throughput and speed in electronics for decades before the earliest claimed priority date of the ’508 patent,” and that a POSA “would have readily understood that [Jones’s] use of parallel ADCs for simultaneously measuring multiple impedances would have advantageously enabled increased throughput for achieving millisecond-time resolution measurements.” Pet., 41-42.

The Petition further explained that Jones’s stated purposes and advantages (*e.g.*, enabling temperature control in a compact form factor) *bolster* a POSA’s motivation to use Jones—they do not detract from it. Pet., 43-44; EX1003, ¶121. Agilent’s argument that Jones’s advantages would somehow dissuade a POSA from using Jones has no merit.

C. Agilent Misrepresents The Petition’s Arguments And Jones’s Disclosure.

The POR attempts to muddy the waters by misrepresenting the Petition’s arguments. Agilent argues that Axion “misinterprets the ‘millisecond time resolution’ limitation to simply mean the time required to take one measurement of the impedance of a single well.” POR, 2, 20, 23. Axion already addressed this

misrepresentation (*see* Paper 7 at 3-4), and the Board did not understand Axion to be making this argument. DI, 9-10 (citing Pet., 14, 53). Agilent’s argument is simply wrong. *See, e.g.*, Pet., 53.

Agilent also argues: “Axion misunderstands that the 68.2 ms discussed by Jones is the time to scan *a single well*, not the time period between two consecutive scans of that well.” POR, 21 (Agilent’s emphasis). This, too, is incorrect. *See, e.g.*, EX1003, ¶70 (explaining that the 1.5 second time resolution of Jones’s ¶[0030] is a result of each of eight daughter boards “measuring 16 wells/channels (12 wells plus 4 reference network channels) at 68.2 milliseconds per object (68.2 milliseconds * 16 = 1091.2 milliseconds)”). Axion never argued that Jones’s 68.2 milliseconds is the time between two consecutive measurements of the same well.

Agilent also misrepresents Jones’s disclosure, arguing that Jones does not disclose simultaneous (*i.e.*, parallel) measurements of multiple wells. POR, 11, 22-23. According to Agilent, Jones only uses the term “parallel” with reference to “the physical arrangement of the components of the system.” EX2009, ¶58. As recognized by the Board, that is wrong. DI, 20. Axion’s expert, Dr. Kim, explained that:

Jones explicitly describes an impedance analyzer with parallel ADCs in an impedance measurement system with “massive parallelism, *high temporal sampling*, and a means for interconnecting multiple

microtiter plate sensors to impedance measurement channels” and that such system “*employs parallelism to obtain the required throughput.*”

EX1003, ¶117.

Agilent does not address Jones’s disclosure of “high temporal sampling,” nor does Agilent explain how “employ[ing] parallelism to obtain the required throughput” is not indicative of parallel, simultaneous measurements. Instead, Agilent argues that (i) Jones’s “required throughput” is 1.5 seconds, (ii) Jones does not disclose increasing throughput, and (iii) Jones’s parallelism promotes other purposes, *e.g.*, a compact form factor. POR, 3-7. But even if true, none of these arguments addresses why Jones’s disclosure of “*parallelism to obtain the required throughput*” is allegedly not indicative of parallel, simultaneous measurements.

Agilent also fails to address the Board’s rejection of its argument:

[Jones’s] teachings reasonably suggest that ... [Jones’s] hardware is operated in parallel to measure multiple wells’ impedances at a time

[I]t is unclear what other purpose Jones’s parallel architecture might serve. ... [E]ven if the physical arrangement of daughter boards does provide for a compact form factor[,] ... this does not explain why Jones employs eight daughter boards each with its own measurement circuitry if that circuitry only operates serially on one daughter board at time, as Patent Owner suggests.

DI, 20.

The Board was correct, as the post-institution record confirms. Indeed, Agilent’s post-institution disclaimer of claims 16-22 (which require simultaneous measurements of multiple wells) in view of the Petition’s Xu-752/Jones

obviousness ground is an admission that Jones discloses parallel measurements. EX2020.

III. CLAIM CONSTRUCTION – “MILLISECOND TIME RESOLUTION”

Claim 1 recites, among other features, an impedance analyzer that “monitors the electrode arrays at *millisecond time resolution*.” As explained in the Petition (at 13-14), and as recognized by the Board (DI, 10-11), the ’508 patent’s disclosures are inconsistent with respect to the “millisecond time resolution” limitation: the “Definitions” section suggests that such measurements must occur at less than 300 milliseconds (EX1001, 10:8-24), whereas other specification disclosures (and now-disclaimed claims 9 and 10) state that measurements at 500 milliseconds meet this limitation. *Id.*, 23:52-55, 24:37-39, 39:47-52, 43:27-33, 47:46-51; EX1003, ¶28. The Board encouraged the parties to address this “contradiction in the intrinsic record.” DI, 11. Axion responds to the Board’s request below.

A. Agilent Changed Position With No Explanation.

In the POR, Agilent contends that “the distinction between 300 milliseconds and 500 milliseconds is immaterial to the dispute in this IPR because Jones teaches a 1.5 second update period, thus at least three times longer than the 500 milliseconds formulation.” POR, 14-15. The POR nevertheless proposes using the “less than 500 milliseconds” formulation. *Id.*

Agilent’s POR reverses its position from the POPR (at 11). Agilent’s new “less than 500 milliseconds” construction is also inconsistent with other portions of the POR suggesting that Agilent acted as its own lexicographer in setting forth an express definition having the “less than 300 milliseconds” formulation. *See, e.g.,* POR, 14-15 (arguing that the patent “expressly defines ‘millisecond time resolution’ using the ‘*less than 300 milliseconds*’ formulation”). The POR does not explain (i) the rationale for Agilent’s change in position, or (ii) why the “less than 500 milliseconds” formulation should be applied despite the alleged lexicography using the “less than 300 milliseconds” formulation. The POR also does not address the specific issues the Board raised in the DI.

B. Axion Agrees That, In This IPR, The 300 Versus 500 Milliseconds Distinction Is Immaterial To Addressing the Unpatentability of the Challenged Claims.

As the Petition explains (at 63-65), the Xu-752/Jones combination would have rendered obvious claims 11-14, which require various millisecond time resolutions (of less than 100, 40, 20, and 5 milliseconds, respectively)—all of which are less than both 300 and 500 milliseconds. Axion also agrees that the term “millisecond time resolution” is “the time between two consecutive impedance measurements for each and every well being evaluated in the claimed apparatus or system.” *See* Section II.C above (refuting Agilent’s assertion that “Axion incorrectly argues that” the claim term is “*directed to the time span required to*

take a single measurement of the electrical impedance *of one well*.” POR, 2 (Agilent’s emphasis)).

C. The Board Must Decide Unpatentability Notwithstanding The ’508 Patent’s Indefiniteness Issues.

While the Board need not resolve the contradiction in the intrinsic evidence regarding the 300 versus 500 milliseconds distinction to decide the unpatentability of the challenged claims, Axion responds to the issues raised in the DI.

First, column 10, lines 13-15 of the ’508 patent should not be treated as definitional. The standard for finding lexicography is “exacting,” *GE Lighting Solns, LLC v. Agilight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014), and it requires “sufficient clarity to put one reasonably skilled in the art on notice that the inventor intended to redefine the claim term.” *Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1370 (Fed. Cir. 2005).

Here, a POSA would not have been put on notice that the inventors intended to define the “millisecond time resolution” limitation as being less than 300 milliseconds in view of the patent’s contradictory statements suggesting that less than 500 milliseconds is sufficient. Indeed, Agilent’s change in position from the POPR to the POR only underscores the ambiguity and lack of lexicography. Further, there is additional evidence of an indefiniteness problem—Agilent’s Dr. Sanchez’s testified that any measurements of less than one second would meet the “millisecond time resolution” limitation. EX1028, 50:20-51:14.

Second, now-disclaimed dependent claims 9 and 10 support that there is no lexicography. “The public is entitled to rely upon the public record of a patent in determining the scope of the patent’s claims,”⁸ and courts have thus recognized that a statutory disclaimer does not render the disclaimed claims irrelevant in construing other claims. *See, e.g., Allergan Sales, LLC v. Sandoz, Inc.*, No. 2:12-CV-00207, 2013 WL 4854786, *6 (E.D. Tex. Sept. 4, 2013). Here, claims 9 and 10 (reciting “less than 500 milliseconds” and “between 500 and 100 milliseconds,” respectively) are inconsistent with the “less than 300 milliseconds” formulation, further showing that the exacting standard for lexicography is not met.

Finally, notwithstanding these indefiniteness issues, the Board must decide the unpatentability of the challenged claims. Under 35 U.S.C. § 318(a), the Board “shall” issue a final written decision addressing the patentability of every challenged claim, and the Federal Circuit has confirmed that this mandate is excused “only when the indefiniteness renders it logically impossible for the Board to reach such a decision.” *Intel Corp. v. Qualcomm Inc.*, 21 F.4th 801, 813 (Fed. Cir. 2021). Because the parties here agree that the claims’ unpatentability can be determined without resolving the 300 versus 500 milliseconds indefiniteness issue,

⁸ *Vectra Fitness, Inc. v. TNWK Corp.*, 162 F.3d 1379, 1384 (Fed. Cir. 1998).

this case falls outside the “logically impossible” exception. Accordingly, the Board must decide the merits of Axion’s unpatentability challenge.

IV. CONCLUSION

The Board should cancel claims 1-8 and 11-15 of the ’508 patent.

Respectfully submitted,

Dated: September 11, 2025

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), the undersigned certifies that on September 11, 2025, a complete and entire copy of PETITIONER'S REPLY TO PATENT OWNER'S RESPONSE has been served in its entirety by e-mail to:

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CERTIFICATE OF WORD COUNT UNDER 37 C.F.R. § 42.24(a)

I, the undersigned, do hereby certify that the attached petition contains 5,597 words, as measured by the Word Count function of Microsoft Word. This is less than the limit of 5,600 words as specified by 37 C.F.R. § 42.24(c)(i).

Respectfully submitted,

Dated: September 11, 2025

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