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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AXION BIOSYSTEMS, INC.,

Petitioner,

v.

AGILENT TECHNOLOGIES, INC.,

Patent Owner.

Case No. IPR2024-01467

Patent 11,906,508

PATENT OWNER SUR-REPLY

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PATENT OWNER'S EXHIBIT LIST

Pursuant to 37 C.F.R. § 42.63(e), Patent Owner Agilent Technologies, Inc. hereby submits its exhibit list associated with the above-captioned *inter partes* review of U.S. Patent No. 11,906,508.

Ex. 2001	Statutory Disclaimer in a Patent Under 37 C.F.R. 1.321(a)
Ex. 2002	File History of U.S. Patent No. 11,906,508
Ex. 2003-1	File History of U.S. Patent No. 9,709,548 (pp. 1-263)
Ex. 2003-2	File History of U.S. Patent No. 9,709,548 (pp. 264-551)
Ex. 2003-3	File History of U.S. Patent No. 9,709,548 (pp. 552-862)
Ex. 2003-4	File History of U.S. Patent No. 9,709,548 (pp. 863-1115)
Ex. 2003-5	File History of U.S. Patent No. 9,709,548 (pp. 1116-1316)
Ex. 2004	Declaration of Brian T. Cunningham, Ph.D. (withdrawn on 7/22/25, <i>see</i> Ex. 3001)
Ex. 2005	<i>Curriculum Vitae</i> of Brian T. Cunningham, Ph.D.
Ex. 2006	Graf, Modern Dictionary of Electronics (1999) (excerpts)
Ex. 2007	File History of U.S. Patent No. 7,459,918 (Jones)
Ex. 2008	File History of U.S. Patent No. 7,192,752 to Xu et al. ("Xu-752")
Ex. 2009	Declaration of Benjamin Sanchez Terrones, Ph.D.
Ex. 2010	<i>Curriculum Vitae</i> of Benjamin Sanchez Terrones, Ph.D.
Ex. 2011	MDS Sciex - CellKey Brochure (c. 2005)
Ex. 2012	CellKey Specifications (2007)
Ex. 2013	CellKey Press Release (2005)
Ex. 2014	U.S. Patent App. Pub. No. 2008/0043448A1 (Finnerty)
Ex. 2015	U.S. Patent App. Pub. No. 2008/0068790A1 (Lee)
Ex. 2016	U.S. Patent App. Pub. No. 2008/0037218A1 (Sharma)
Ex. 2017	U.S. Patent App. Pub. No. 2008/0298014A1 (Franco)
Ex. 2018	U.S. Patent App. Pub. No. 2008/0257594A1 (Engblom)
Ex. 2019	U.S. Patent App. Pub. No. 2008/0304223A1 (Franz)
Ex. 2020	2nd Statutory Disclaimer in a Patent Under 37 C.F.R. 1.321(a)

Ex. 2021	Declaration of Yang Wang, Ph.D., Esq.
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Ex. 2023	D. Ct. Docket – Claim Construction Rulings (highlighted)
Ex. 2024	Handbook & Selection Guide for Computer-Based Data Acquisition & Control Systems (Neff) (2007)
Ex. 2025	Current Biosensor Technologies in Drug Discovery (Cooper) (2006)
Ex. 2026	Label-Free Biosensors - Electrical impedance technology applied to cell-based assays (McGuinness & Verdonk) (2009)
Ex. 2027	Cellular Dielectric Spectroscopy - A Label-Free Comprehensive Platform for Functional Evaluation of Endogenous Receptors (Verdonk) (2006)
Ex. 2028	Enhanced Selectivity Screening of GPCR Ligands Using a Label-Free Cell (McGuinness) (2009)
Ex. 2029	U.S. Pat. App. Pub. No. 2007/0087326A1 (Minor)
Ex. 2030	Cellular Dielectric Spectroscopy, A Powerful New Approach to Label-Free Cellular Analysis (2004) (Ciambrone)
Ex. 2031	Cellular Dielectric Spectroscopy - A Label-Free Technology for Drug Discovery (Leung) (2005)
Ex. 2032	U.S. Pat. App. Pub. No. 2009/0093011A1 (Fang)
Ex. 2033	U.S. Pat. No. 9,121,806 (Bhansali)
Ex. 2034	U.S. Pat. App. Pub. No. 2011/0195436A1 (Moreau)
Ex. 2035	Evaluating Cellular Impedance Assays for Detection of GPCR Pleiotropic Signaling and Functional Selectivity (Peters) (2009)
Ex. 2036	Monitoring fibroblast behavior in tissue culture with an applied electric field (Giaever) (1984)
Ex. 2037	Microplate Dimensions Guide (2007)

I. INTRODUCTION

The Board’s Decision on Institution (“DI”) correctly identified the fundamental flaw in Axion’s case: Axion’s Petition and Dr. Kim’s declaration (Ex. 1003) provide insufficient reasoning why a POSA would have made “Dr. Kim’s examples [that] modify multiple aspects of Jones’s 96-well embodiment”. DI at 23. As the Board postulated, “the parameters for Dr. Kim’s examples were chosen not because they were obvious, but because they would result in a time between measurements of 500 milliseconds or less” *Id.* at 24. Axion’s Reply does not respond to the Board’s concerns and does not cure this fatal defect. Instead, Axion’s Reply further demonstrates that Axion’s arguments are “improperly premised on hindsight knowledge of the ’508 patent as opposed to what Jones teaches or reasonably suggests to a POSA regarding the ‘millisecond time resolution’ limitation.” *Id.* at 25. Axion’s Reply offers no additional expert testimony from Dr. Kim. Instead, Axion simply attempts to supplement Dr. Kim’s deficient declaration with more attorney argument, which is no substitute for expert testimony. *Id.* Axion’s attorney argument cannot take the place of evidence in the record. MPEP § 716.01(c).

Agilent’s post-DI statutory disclaimer of Claims 16–22 (Ex. 2020) was a voluntary response to the Board’s guidance in the DI, narrowing the issues in this proceeding to the parties’ principal dispute—the patentability of the claimed

multiwell cell-based assay system with “millisecond time resolution”. Agilent did not concede that Claims 16–22 are unpatentable. In sharp contrast, Axion has failed to respond substantively to the Board’s concerns articulated in the DI, instead merely reiterating Axion’s initial flawed arguments based on Dr. Kim’s unsupported “examples”.

In addition, in an apparent recognition of the weakness of Jones with respect to the key “millisecond time resolution” limitation, Axion now endeavors to introduce a new implicit ground of unpatentability in its Reply, relying on a previously filed but largely neglected reference to Ghosh (Ex. 1017). Of course, Axion is not permitted to add a new unpatentability ground on reply. 37 C.F.R. § 42.23(b). As discussed below, Ghosh does not cure Axion’s fatally defective arguments and is an even weaker reference than Jones.

II. DR. KIM’S DECLARATION REMAINS DEFICIENT

A. Axion’s Attorney Argument Cannot Cure Dr. Kim’s Failure To Explain *Why* A POSA Would Have Purportedly Made So Many Unsuggested Modifications To Jones’ ZMS To Achieve Millisecond Time Resolution

In its DI, the Board found that “[i]nstead of relying on the 96-well embodiment in Paragraph 30, or any other embodiment expressly described in Jones, Petitioner relies on ‘*examples*’ evidenced by Dr. Kim’s testimony and based on modifications of the 96-well embodiment taught in Jones.” DI at 23 (emphasis added). The Board further found that Axion’s and Dr. Kim’s reasoning for

modifying Jones' system was "not explained sufficiently in the Petition." *Id.* at 23-24. Despite this clear invitation from the Board, Axion failed to provide any explanation of why Dr. Kim modified multiple aspects of Jones' 96-well embodiment by "reducing both the total number of wells and wells per row to an '8 x 2 configuration,' reducing the number of reference channels from four to three, and further for the single frequency example changing from a 'stepped sweep' of multiple frequencies to a single measurement at 10 kHz." *Id.* The Board further correctly noted that "such **cherry-picking** suggests that Petitioner's showing for claims 1–8 and 11–15 is **improperly premised on hindsight knowledge of the '508 patent** as opposed to what Jones teaches or reasonably suggests to a POSA regarding the 'millisecond time resolution' limitation." *Id.* at 24-25 (emphases added).

Axion's only response to the Board's clearly expressed concerns was simply more attorney argument, essentially asking the Board to re-read Dr. Kim's Declaration, but this time, to reach the opposite conclusion. Arguments presented by a party, via its attorneys, cannot take the place of evidence in the record. *See Apple Inc. v. LBT IP I LLC*, IPR2020-01191, Paper 39, at 29 (PTAB Mar. 2, 2022) ("Patent Owner's arguments disputing Mr. Andrews' testimony on an ordinarily skilled artisan's understanding of Sakamoto are attorney argument only and are unsupported by any record evidence. ***These attorney arguments are entitled to***

little, if any, weight.”) (emphasis added); *Qualcomm Inc. v. UNM Rainforest*

Innovations, IPR2021-00582, Paper 63, at 16-17 (PTAB Aug. 15, 2022)

(“Argument of counsel cannot take the place of objective evidence”). The Board raised specific concerns about fundamental deficiencies in Dr. Kim’s testimony, and Axion’s attorney argument is insufficient to cure the fatal deficiencies in Dr. Kim’s testimony.

In its Reply, Axion argues that “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.” Reply at 2. But Axion provided no such “documentary evidence”, and Dr. Kim’s results-oriented concocted “examples” are not supported by the Jones reference itself. *See Sony Interactive Entertainment LLC v. Quantum Imaging, LLC*, IPR2023-00995, Paper 53, at 25 (PTAB Dec. 9, 2024) (finding expert testimony was “entirely without support either in [the prior art reference] or from any persuasive supporting reference or evidence that it was known, at the time of filing of the application which became the [challenged] patent.”).

It is unsurprising that Axion did not respond substantively to the Board’s focused query because, with respect to the “millisecond time resolution” dispute, there is nothing more in Jones than a succinct, single-paragraph, 135-word discussion about its system’s “target 1.5 second update period”. Simply

concocting additional unsupported examples by reconfiguring the Jones device would not have addressed the key inquiry—*why* a POSA reading Jones would have understood that such hypothetical modifications would be implemented to achieve millisecond time resolution?

In its Reply, Axion argues that “Jones also describes other configurations that would have a faster update period” and “Agilent errs in failing to consider the alternative configurations that Jones discloses or suggests to a POSA.” Reply at 3-4. But those arguments are again facially incorrect. Jones only describes a single embodiment at Paragraph 30 with a “target 1.5 second update period.” No other “alternative configurations” are described or discussed in Jones. And given that Jones does not discuss any applications for its ZMS (“Impedance Measurement System”), there would be no reason for a POSA to perceive any “alternative configurations” when reading Jones. Of course, the unpatentability grounds in this IPR proceeding are Xu-752 + Jones, *not* Xu-752 + Jones + Dr. Kim.

B. Dr. Kim’s “Examples” Are A Hindsight-Driven Hypothetical Recreation Of Jones’ ZMS

Jones provides a 135-word disclosure at Paragraph 30 discussing an embodiment of MDS Sciex’ compact ZMS: a 1.5-second update period for a 96-well plate. Dr. Kim’s declaration, by contrast, contorts this single example into multiple, complex, and undisclosed configurations spanning many pages of

calculations and tables, including a myriad of “examples” based on unwarranted modifications to the 96-well embodiment in Jones. *E.g.*, Ex. 1003 ¶¶ 72, 137, 139, 173, 175. In its Reply, Axion relies almost exclusively on **Dr. Kim’s** examples, not the disclosure in Jones itself:

Dr. Kim’s examples apply different configurations of Jones’s impedance 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).

Reply at 5-6. Notably, Axion acknowledges that these are “Dr. Kim’s examples” and not examples from Jones. *Id.*; *see* PTAB Consolidated Trial Practice Guide, at 36 (Nov. 2019) (“[E]xpert testimony cannot take the place of disclosure from

patents or printed publications. In other words, expert testimony may explain ‘patents and printed publications,’ but is not a substitute for disclosure in a prior art reference itself.”). Also, while Jones teaches “a series of single frequency bursts—one burst for each selected frequency” (Ex. 1006 ¶ [0030]), Jones does not specify those applied frequencies, nor the “10, 50, or 100 kHz” frequencies devised by Dr. Kim in his “examples” above. *E.g.*, Ex. 1003 ¶¶ 71-75.

Dr. Kim’s many mathematical contortions are not a simple explanation of Jones, which is the proper role of an expert witness, but instead a clear attempt to drastically expand and revise Jones’ teachings using hindsight gleaned from the ’508 patent as a target. A proper obviousness evaluation is directed to what the prior art would have taught or suggested to a POSA at the time of the invention, not what an expert witness can expand from the reference some 15 years later in attempt to satisfy a challenged claim limitation.

C. Agilent Repeatedly Contested Dr. Kim’s Testimony

In its Reply, Axion incorrectly argues that “Dr. Kim’s testimony about these configurations is uncontested” and “Agilent does not contest any of these points, nor could it”. Reply at 4-5. Contrary to Axion’s arguments, Agilent expressly contested Dr. Kim’s extensive, concocted mathematical configurations by (a) contrasting Dr. Kim’s testimony with the simple, single-paragraph disclosure of Jones itself (Ex. 1006 ¶ [0030]), (b) providing the detailed rebuttal testimony of

Dr. Sanchez (Exs. 2009 & 1028), and (c) setting forth in Agilent’s POR the detailed explanations about what Jones would (and would not have) taught or suggested to a POSA (*e.g.*, POR at 14-17). Further, in his declaration, Dr. Sanchez explained that Dr. Kim’s examples were nowhere suggested in Jones and would not have been contemplated by a POSA. Ex. 2009 ¶ 52. Dr. Sanchez correctly explained that Jones teaches a single, specific example of scanning all the wells in a 96-well plate in 1.5 seconds. *Id.* ¶¶ 37, 40-42. Jones nowhere teaches or suggests the allegedly faster configurations that Dr. Kim contrives. *Id.* ¶¶ 34–37, 52. Indeed, Dr. Sanchez even concludes that “I have reviewed Dr. Kim’s lengthy analysis, and in my opinion it is an exercise in hindsight reconstruction in an attempt to meet the limitations of the ’508 Patent’s claims”. *Id.* ¶ 52. Dr. Sanchez further confirmed his analysis during his cross-examination. Ex. 1028 at 93:22 – 94:8. In Agilent’s POR, relying on Dr. Sanchez’ expert opinions, Agilent also contested Dr. Kim’s contrived “examples”, explaining that those calculations and tables were nothing more than hindsight reconstructions entirely divorced from Jones’ actual disclosure. POR at 14-17, 22.

Axion further incorrectly argues that “having failed to challenge [Dr. Kim’s] examples showing Jones’s capability of providing millisecond time resolution measurements, Agilent has waived any contrary arguments”, citing “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).” Reply at 6.

Agilent chose not to depose Dr. Kim because his declaration testimony was glaringly deficient on its face, and had already been suggested as such by the Board in the DI. The PTAB’s Rules do not require that a party cross-examine an opposing expert, and the authority cited by Axion says nothing of the kind. In particular, the Scheduling Order does not impose any obligation for either party to cross-examine the other party’s expert witness. Scheduling Order, Paper 10, § A.5. And in the *Google* case cited by Axion, the Board determined that a **credibility** challenge was “untimely and forfeit” because “it was not raised in the Response and is not fairly responsive to the Reply.” *Google*, Paper 76, at 14. Here, Agilent does not challenge Dr. Kim’s credibility, but rather the substance of his testimony in attempting to dramatically expand the scope of Jones’ disclosure, which had already been questioned by the Board. And as explained above, Agilent has consistently challenged Dr. Kim’s testimony with regard to his many hypothetical modifications to Jones’ single-paragraph, 135-word discussion about its system’s “target 1.5 second update period”.

“Courts have uniformly rejected the [argument] that the failure to depose an expert affects the right to object to the expert’s testimony.” *Hinton v. Outboard Marine Corp.*, 828 F. Supp. 2d 366, 370 (D. Me. 2011) (citing, *inter alia*, *Bonesmo v. The Nemours Found.*, 253 F. Supp. 2d 801, 811 (D. Del. 2003) (“Contrary to

plaintiffs' argument, the opposing party is ***not required*** to depose the expert to develop what his opinion is or the reasons for it.") (emphasis added)). Thus, Agilent's choosing not to cross-examine Dr. Kim was not any kind of concession, admission, or waiver, as Axion incorrectly asserts.

III. JONES DOES NOT TEACH OR SUGGEST THE CLAIMED "MILLISECOND TIME RESOLUTION"

A. Jones' Single Embodiment Is A Compact ZMS With A "Target 1.5 Second Update Period"

Axion's argument that Jones "suggests" other configurations ignores the reality that Paragraph 30 is the ***only*** teaching that provides any throughput or update period information for Jones' compact ZMS. Ex. 1006 ¶ [0030]. The alternative parameters that Axion cites (*e.g.*, using a single frequency or using fewer reference channels) are not discussed in the context of Paragraph 30 or related to the ZMS' update period. A POSA would simply have understood that Jones' disclosure taught a "target 1.5 second update period", not "millisecond time resolution" (*i.e.*, less than 500 milliseconds). Ex. 2009 ¶¶ 52, 54, 56.

Indeed, the missing "millisecond time resolution" limitation in Jones is evident from Axion's own arguments:

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 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>

Reply at 8-9. Glaringly absent from Axion's above claim chart is the key "millisecond time resolution" limitation.

B. Agilent In No Way "Concedes That Configurations [Contrived By Dr. Kim] Would Have A Millisecond Time Resolution"

In its Reply, Axion incorrectly argues that Agilent somehow "concedes that configurations described in Jones would have a millisecond time resolution".

Reply at 4. To the contrary, Agilent has consistently—and correctly—maintained that Jones does **not** teach an impedance measurement system having a millisecond time resolution. *See supra* Section II.C. To be clear, Jones does not teach "configurations" (plural) but rather discloses only a single embodiment, and in that

example the throughput time is—by design—1.5 seconds, the “target” time to satisfy the required throughput specification. *Id.*

C. Axion Ignores Jones’ Express Teaching Of “The *Target* 1.5 Second Update Period”

The lone Paragraph 30 in Jones example plainly states that the disclosed ZMS has a “*target* 1.5 second update period”. Ex. 1006 ¶ [0030]. Jones also refers to this target update period as “the required throughput” of the ZMS. *Id.* ¶ [0006]. There is no teaching or suggestion in Jones of reducing the update period below the target 1.5 seconds. As Agilent explained in its POR, this target 1.5 second throughput is consistent with the commercial CellKey impedance analyzer system sold by MDS Sciex, the assignee of the Jones application. POR at 5-6; Exs. 2011-2013. Axion’s only response to that contemporaneous evidence is that “Agilent’s Exs. 2011-2013, indicating 2-10 second update periods for a 96-well plate in MDS Sciex’ commercial product, are beside the point.” Reply at 7, n.3.

Axion hopes to sidestep this contemporaneous evidence, which Dr. Sanchez explains provides a POSA’s understanding of the state-of-the-art in the 2008-2009 time frame. Ex. 2009 ¶ 41. In particular, the concluding sentence in Jones Paragraph 30 is significant to gain an understanding how a POSA would have understood Jones’ teaching. *Id.* Throughout the Jones disclosure, Jones’ sole focus was on developing a ZMS with a smaller form factor that could effectively

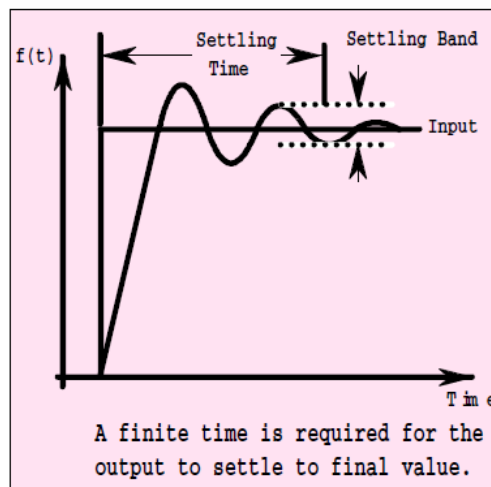
manage the additional heat generated by the more compact physical configuration with closely spaced parallel components. *Id.* ¶¶ 59-61. Jones nowhere expresses any desire for its ZMS to **increase** throughput, and a POSA would not have understood any such teaching in Jones. *Id.* ¶ 53. Jones' stated goal was to design a more compact system that would maintain specified throughput to the then-existing larger commercial systems, such as the CellKey system. *Id.* ¶¶ 55-56, 59. Indeed, Jones' goal of providing a "target" 1.5 second update period for the ZMS is shown in his express calculations, where he **adds** a remainder amount of "multiplexer switching and signal settling" time to the calculated "measurement period" in order for the total update period to be 1.5 seconds. Ex. 1006 ¶ [0030] ("calculations to determine sufficient samples suggest a 1091 mS measurement period, **leaving** 409 mS for multiplexer switching and signal settling within the target 1.5 second update period.") (emphasis added).

In Jones' multiplexed ZMS, "[d]uring gain switching and well selection, transients are generated" Ex. 1006 ¶ [0033]. The "target 1.5 second update period" includes time for "well and gain multiplexer switching transients to settle and to obtain the necessary number of sample points." *Id.* ¶ [0030]. Thus, multiplexer switching and signal settling time would have been important in Jones' multiplexed system, and longer settlement times would be necessary to maintain

system accuracy.¹ *See* Ex. 2009 ¶ 42 (“electrical transients occurring after each multiplexer switching operation between wells and reference channels within a row in the microtiter plate.”); Ex. 1028 at 93:22 – 93:1 (“[W]ith reduced measurement times there is a compromise on measurement accuracy, right? And

¹ It was well-known that in a multiplexed system, longer settlement times would be necessary to achieve acceptable accuracy:

Settling Time. The time interval between the application of an input and the time when the output is within an acceptable band of the final steady-state value.



High sampling rates. With an ADC per channel, the sampling rate is not encumbered with considerations such as multiplexing and post-amplifier settling time.

Ex. 2024 at 164, 175.

part of my PhD was precisely to move forward the body of knowledge and scientific knowledge to balance this trade off”).

Importantly, Jones’ teaching of “**leaving** 409 mS for multiplexer switching and signal settling” demonstrates that the 409 milliseconds is not a calculated value or some minimum amount of time, but instead is the maximum amount of time allowable to maintain “the target 1.5 second update period.” As Dr. Sanchez explained:

Axion asserts, again incorrectly, that “for a multi well plate having even fewer wells, or where the user only wanted to monitor a more limited number of wells in a 96-well plate, Jones discloses providing a higher measurement rate with less time between two measurements in each well.” Pet. at 36. It is my opinion that Jones nowhere “discloses providing a higher measurement rate” or “monitor[ing] a more limited number of wells”. To the contrary, Jones explains that the specification to meet (or the “target update period”) is 1.5 seconds. Thus, ***Jones allocates any time after the individual well measurements “for multiplexer switching and signal settling”.***

Ex. 2009 ¶ 37 (emphasis added).

Dr. Kim’s pervasive assumption in his many pages of contrived examples is that Jones’ “multiplexer switching and signal settling” time is somehow a constant or a fixed value, which finds no support in Jones’ express teachings. *Id.* To the

contrary, the “multiplexer switching and signal settling” time is simply the maximum amount of time allowable so that, when added to the “measurement period” time, “the target 1.5 second update period” can be achieved. *Id.* And a POSA would have added as much settling time as possible to minimize the signal perturbations and noise resulting from the system’s repeated multiplexing switching. *Id.* Jones nowhere teaches or suggests a target update period of less than 1.5 seconds. *Id.* ¶¶ 34-37, 40-42, 52. Consequently, a POSA would have understood that Jones’ ZMS was a 1.5 second throughput system, and Dr. Kim’s hand-waving and contrived examples are nothing more than blatant hindsight reconstructions, attempting to create a system that Jones nowhere taught and a POSA would not have envisaged from Jones’ disclosure. *Id.*

D. Skilled Artisans Would Not Fabricate Different-Than-Specified System Update Rates Based Upon Contorted Frequency Calculations

In its Reply, Axion relies exclusively on pages of calculations and tables crafted by Dr. Kim. Employing various hypothetical combinations of frequencies, Dr. Kim then contrives different update periods, with his acknowledged goal (*i.e.*, hindsight endeavor) of devising a possible shorter-than-specified system update period, namely, shorter than Jones’ expressly specified “target 1.5 second update period”—classic hindsight reconstruction.

While apparently Jones’ ZMS was never commercialized, when Jones, et al. filed their patent application in 2005, the application’s assignee (MDS Sciex) had commercialized its impedance-based measurement system called the “CellKey System”. Exs. 2011, 2013. As noted in Agilent’s POR, the CellKey System had a specified update rate of 2 or 10 seconds and a specified measurement frequency range of 1 kHz – 10 Mhz:

Measurement Frequency Range	1 kHz - 10 MHz
* * *	
Update Rate 96-well	2- or 10-second update rate

Ex. 2012 at 1.



Figure 6 The CellKey™ System from MDS Sciex

Ex. 2025 (Cooper) (2006) at 14.

A review of the contemporaneous discussions of the CellKey System (including by MDS Sciex itself) readily reveals that—unlike Dr. Kim—skilled artisans did *not* endeavor to contrive different-than-specified system update rates based upon contorted frequency calculations:

We designed a system capable of producing impedance measurements simultaneously across a large range of frequencies (from 1 kHz to 10 MHz) before, during, and after receptor activation. This approach facilitates *the measurement of early events within seconds to minutes* of ligand addition in receptor signaling cascades.... (15 min assay with *2 s update rate*).

Ex. 2026 at 256, 259 (emphases added).

Small-amplitude AC voltage at 24 frequencies, from 1 KHz to 10 MHz, is applied to a monolayer of cells, and the resultant current is measured at an *update rate of 2 s*.... The *quick update rate (2 s)* of the CellKey system allows detection of these *immediate changes in impedance*.

Ex. 2027 at 611 (emphases added).

The instrument applies small voltages at 24 discrete frequencies, from 1 kHz to 10 MHz, once every 2 s.... 10 min of cellular activation were recorded at an *update rate of 2 s* per 96 wells.

Ex. 2028 at 813-15 (emphasis added).

The electrical impedance of the cells was measured using CellKey™ (MDS Sciex, Concord, Ontario) *according to the protocol of the*

manufacturer [Ex. 2030]. In particular, 100 mV voltage was applied to the cells with a sweeping frequency range of 1 kHz to 10 MHz.

Ex. 2029 ¶ [0069] (emphasis added) (referencing Ex. 2030 (prototype CellKey)); *see, e.g.*, Ex. 2031 (prototype CellKey) at 266 (similar); Ex. 2032 ¶ [0060] (“The system operates using a small-amplitude alternating voltage at 24 frequencies, from 1 KHz to 10 MHz. The resultant current is measured at an *update rate of 2 sec.*”) (emphasis added); Ex. 2033, Col. 2:34-38 (“[C]hanges in cellular bio impedance are *collected every two seconds* as spectrum of frequencies (1 KHz to 10 MHz).”) (emphasis added); Ex. 2025 at 14 (same); Ex. 2034 ¶ [0069] (“Small voltage at 24 frequencies, from 1 KHz to 10 MHz, is applied ... and the resultant current is measured at an *update rate of 2 s.*”) (emphasis added); *id.* ¶ [0067] (“The quick *update rate (2 s.)* of the CellKey™ system allows detection of these *immediate changes in impedance.*”) (emphases added); Ex. 2035 at 247 (“5 min, *2-sec intervals*”) (emphasis added).

Thus, the contemporaneous evidence demonstrates that skilled artisans readily understood that the MDS Sciex’ CellKey System had a measurement frequency specification of 1 kHz – 10 Mhz, performed measurements at multiple stepped frequencies, and had an update rate of 2 seconds (or longer). *Id.* A POSA would have similarly understood that the MDS Sciex ZMS in Jones had an unspecified measurement frequency range and an update rate of 1.5 seconds. Ex.

1006 ¶ [0030]; Ex. 2009 ¶¶ 37, 52. As exemplified above, A POSA would not have endeavored to create different-than-specified system update rates based upon concocted frequency calculations.

E. Axion’s Unsupported Arguments That Jones Was “Capable” Of Millisecond Time Resolution Are Legally Deficient

In its Reply, Axion repeatedly argues that Jones, per Dr. Kim’s elaborate modifications, would have been “capable” of performing a faster update period. *E.g.*, Reply § 2 (heading). Even if Axion’s allegation were true, simply arguing that a device would have been *capable* of performing the claimed invention, without adequately explaining *why* a POSA would have been motivated to make the proposed modifications, is insufficient to render the invention obvious:

Here, Qualcomm failed to put forth any argument or evidence in its petitions as to whether [the prior art] device, even if capable of doing so, actually would output [conditions as described by the claim limitation], or why a person of ordinary skill in the art would have been motivated to use the particular inputs that would result in such an output, choosing to broach that subject for the first time in its reply briefs.

ParkerVision Inc. v. Qualcomm, Inc., 903 F.3d 1354, 1363 (Fed. Cir. 2018).

Axion provides no such explanation here.

IV. AXION’S NEW RELIANCE ON GHOSH IS UNAVAILING

A. Axion Cannot Add A New Unpatentability Ground On Reply

In its Reply, Axion attempts to introduce Ghosh (Ex. 1017) as a new ground of unpatentability. *See* Reply at 12 (“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.”) (emphases in original). “Petitioner may not submit new evidence or argument in Reply that it could have presented earlier, e.g. to make out a prima facie case of unpatentability.” PTAB Consolidated Trial Practice Guide, at 73; *see Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369-70 (Fed. Cir. 2016) (The Board did not abuse its discretion in refusing to consider reply brief arguments advocating a “new theory” of unpatentability under 37 C.F.R. § 42.23(b).). Axion’s use of Ghosh on reply is an impermissible attempt to salvage a deficient obviousness case with a reference not relied upon by Axion in its Petition (*viz.*, Xu-752 + Jones). *Id.*; *see Henny Penny Corp. v. Frymaster L.L.C.*, IPR2016-01435, Paper 47, at 17 (PTAB Dec. 21, 2017) (“We disregard Petitioner’s alternative position as it was an attempt to raise a new theory of unpatentability improperly for the first time in the Reply.”).

B. Ghosh Describes An Entirely Dissimilar Single-Sample System For Studying Electroporation In A Large Tissue Culture Dish

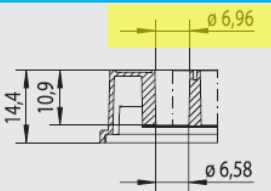
Ghosh describes a single-sample system for “the measurement of pore formation and closure in anchored mammalian cells”, called “electroporation”. Ex. 1017, Abstract. Ghosh measures when “small transient pores are formed in the membrane” by applying a “low voltage (1V-5V) pulse” using a single sample of cells growing on a “[p]olystyrene dish (60 mm) of tissue culture optical quality....” *Id.* at 1063-64; Ex. 2036 at 3761; Ex. 1017, Abstract (“[T]he application of a few volts across the cell-covered electrode causes pore formation in the cell membrane.”). While Axion acknowledges that Ghosh is used for “measuring *a single sample*” (Reply at 12 (emphasis added)), Axion entirely ignores that a POSA designing the multi-well impedance-based cellular assay system described and claimed in the ’508 Patent would not have looked to Ghosh in that endeavor, at least because Ghosh is directed to a very different analysis and uses an entirely dissimilar system. The ’508 Patent nowhere discusses electroporation (“the formation and resealing of pores due to applied electric fields”) or electropermeabilization (when “a normally selective biological membrane suddenly becom[es] permeable to a wide variety of ions and molecules under influence of a strong electric field.”) (Ex. 1017 at 1602), and likewise nowhere mentions membrane “pores” or “permeability”. The 2 square centimeter

dimensions of the large electrode used in Ghosh would not be compatible with the micron or millimeter electrode dimensions (Ex. 1001, Col. 14:45-50) or millimeter microtiter plate well dimensions (*id.*, Col. 23:24-30) described in the '508 patent.

Ghosh is also very dissimilar to Jones and Xu. Jones is directed to “[a]n impedance measurement system for measuring the complex impedance of each well of a microtiter plate, the microtiter plate wells being formed in an array of rows and columns” Ex. 1006, Claim 1. Xu is also directed to analysis of cells growing in multiple wells on a microtiter plate. A typical microtiter plate well would have been about 7 millimeters in diameter,² with multiple cell samples growing thereon, which is an order of magnitude smaller than Ghosh’s very different single-sample 60-millimeter tissue culture plate. The 2 square centimeter dimensions of the large electrode of Ghosh would be incompatible with the

² The dimensions for an example microtiter plate are shown below:

96 Well UV-Star® Microplates

F-bottom / chimney well			
			
		- Footprint (length x width): - A1 Row offset: - A1 Column offset: - Well spacing (center to center): - Flange or skirt height: - Mathematical volume: - Working volume:	127.76 x 85.48 mm 11.24 mm 14.38 mm 9.0 mm 2.5 mm 392 µl 25-340 µl
µClear® bottom, clear			
Cat. No.	Description	Qty./bag	Qty./case
655 801	F-bottom / chimney well, µClear® bottom, non-sterile	10	40

Ex. 2037 at 4.

millimeter dimensions of the wells in a microtiter plate. And Jones employs very small voltages, teaching that “[a]ctual well drive will be of the order of 100 mV peak to peak to maximize signal levels without introducing significant distortion” (Ex. 1006 ¶ [0029]), which is also an order of magnitude less than the 1V-5V applied in Ghosh to open the pores on biological membranes. Of course, because Jones is not directed to electroporation or electropermeabilization, Jones does not discuss membrane “pores” or “permeability”. Therefore, the systems, materials, and purposes of Ghosh and Jones were very different.

Ghosh does not describe a system capable of performing impedance measurements across *multiple* wells or any kind of application for high-throughput screening. Ghosh lacks any suggestion to scale up the single-sample system, which uses a large electrode and a large tissue culture plate, to a much more complex, multiwell system. Thus, Axion’s belated attempt to combine Ghosh reference with Jones and Xu still fails to disclose the key “millisecond time resolution” claim limitation.

C. The 15-Year Time Span Between Ghosh And The ’508 Patent Suggests That The Claimed Invention Would *Not* Have Been Obvious

Ghosh was published in 1993, evidencing a 15-year gap between Ghosh and the ’508 Patent (and Jones, for that matter) with no improvement in developing a multi-well assay system for achieving millisecond time resolution. Contrary to

Axion's argument, the 15-year interval without improvement suggests that Agilent's '508 Patent, including the "millisecond time resolution" limitation, would *not* have been obvious. *See Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1359 (Fed. Cir. 2013) ("[T]wenty-two years after Turi and fourteen years after Dikstein ... [t]he intervening time between the prior art's teaching of the components and the eventual preparation of a successful composition speaks volumes to the nonobviousness of [Leo's] patent.").

V. AGILENT PLAINLY EXPLAINED IN ITS POR WHY AGILENT ADOPTED 500 MILLISECONDS FOR PURPOSES OF THIS IPR

In its Reply, Axion incorrectly argues that Agilent failed to explain why it adopted 500ms for purposes of this IPR proceeding. Reply at 22-23. To the contrary, Agilent dedicated Section IV.B of its POR to that explanation:

And particularly important here, 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. Ex. 2009 ¶¶ 33, 40. In the DI, the Board recognized that the distinction between 300 milliseconds and 500 milliseconds is likely not material in this IPR DI at 24-25.

POR at 15.

**VI. AXION’S PERIPHERAL ATTACKS ON DR. SANCHEZ’
TESTIMONY CANNOT WITHSTAND SCRUTINY**

**A. Dr. Sanchez’ Testimony Is Directed To The Missing “Millisecond
Time Resolution” Limitation**

In its Reply, Axion unfairly criticizes Dr. Sanchez’ supposed “rudimentary understanding” of the law of obviousness under 35 U.S.C. § 103. Reply at 12, n.6. But Axion fails to appreciate that Dr. Sanchez, as a technical expert, focused on what the Jones reference would (and would not) have taught or suggested to a POSA in or around 2008. As discussed herein, Dr. Sanchez concluded that Jones and Xu-752, alone or in combination, fail to teach or suggest the “millisecond time resolution,” as expressly recited in Claims 1–8 and 11–15 of the ’508 Patent. *See supra* Section II.C. Thus, there was no need for Dr. Sanchez to consider further whether it would (or would not) have been obvious for a POSA to combine the Xu-752 and Jones references. As Agilent explained in its POR:

Even if Xu-752 and Jones could be properly combined, that combination would not contain each and every element of the invention claimed in the ’508 Patent because it would be missing at least the key “millisecond time resolution” invention claimed in the ’508 Patent.

POR at 7.

B. Dr. Sanchez Was A POSA In The Relevant Time Frame

In its Reply, Axion changes its arguments regarding the relevant time frame for a POSA from Axion's original date of May 2009 to an earlier May **2008** date. Reply at 12, n.7. But as the Board recognized in the DI, and as Agilent relied upon in its POR, Axion's Petition adopted a date of May 2009:

Petitioner contends a person of ordinary skill in the art ("POSA") as of May **2009** Pet. 14 (citing Ex. 1003 ¶¶ 23–25)....

At this stage, we find Petitioner's description of the level of ordinary skill in the art to be sufficiently supported by the record and apply it for purposes of this decision.

DI at 7 (emphasis added).

Not surprisingly, then, Agilent referenced Axion's May 2009 date in its POR, as did Dr. Sanchez in his expert declaration. POR at 9; Ex. 2009 ¶ 17. But both Agilent and Dr. Sanchez recognized that the '508 Patent's priority date was May 2008. POR at 8, 27; Ex. 2009 ¶ 16.

In any event, Axion nonetheless begrudgingly acknowledges that even using its newly argued May 2008 date, Dr. Sanchez still would have been a POSA in the relevant time frame. Reply at 12, n.7 ("To the extent Dr. Sanchez qualified as a POSA as of May 2008 (which Axion does not concede), he did so only barely.").

Moreover, Dr. Sanchez testified that he would have been a POSA in the 2008-2009 time frame. Ex. 2009 ¶ 19; Ex. 1028 at 92:6 – 93:3. And Dr. Sanchez

further testified that his subsequent experimental research and academic experience further informed his understanding of what a POSA would have known and understood in the 2008 time frame. Ex. 1028 at 93:15 – 94:16.

VII. CONCLUSION

For the foregoing reasons and the reasons set forth in Agilent's POR, including the testimony of Dr. Sanchez, Axion has failed to meet its burden of demonstrating that Claims 1–8 and 11–15 of the '508 Patent would have been obvious over Xu-752 and Jones. Accordingly, Agilent respectfully requests that the Board confirm the patentability of Claims 1–8 and 11–15 of the '508 Patent.

Respectfully submitted,

STERLINGTON, PLLC

Dated: October 16, 2025

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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that foregoing Patent Owner Sur-Reply, exclusive of the parts exempted as provided in 37 C.F.R. § 42.24(a), contains 5,585 words and therefore complies with the type-volume limitations of 37 C.F.R. § 42.24(c)(4).

Respectfully submitted,

STERLINGTON, PLLC

Dated: October 16, 2025

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CERTIFICATE OF SERVICE

The undersigned hereby certify that a true and correct copy of the **PATENT OWNER SUR-REPLY** is being served on October 16, 2025, electronically via the Patent Trial and Appeal Case Tracking System (“P-TACTS”) and via electronic mail to the email addresses below:

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