

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

**DECLARATION OF BENJAMIN SANCHEZ TERRONES, Ph.D.,
IN SUPPORT OF PATENT OWNER RESPONSE**

I, Benjamin Sanchez Terrones, Ph.D., being over the age of 18 and competent to make the statements herein, hereby declare that:

I. INTRODUCTION

1. My name is Benjamin Sanchez Terrones, Ph.D. I am currently an Associate Professor in the Department of Electrical and Computer Engineering, Richard and Loan Hill Department of Biomedical Engineering, at the University of Illinois Chicago.

2. As provided in greater detail my *curriculum vitae* (Ex. 2010), I have about twenty-five years of educational, research and industrial experience in electrical engineering and bioengineering. My expertise spans biomedical signal processing, neuromuscular diagnostics, and optimization techniques, with a strong emphasis on translating engineering innovations into medical applications. I have applied electrical and computer engineering principles in health measurement and monitoring for chronic diseases and austere conditions.

3. I have authored or co-authored nearly one hundred peer-reviewed articles, over fifty conference proceedings at international conferences, multiple book chapters, and seminars and conferences talks.

4. My research has been widely recognized through featured publications and media coverage including highlighted articles on *Heart Rhythm*, *Clinical Neurophysiology*, and *IEEE Pulse*. Multiple impedance studies of mine

have been selected as Physiological Measurement's annual Highlights, with several rankings among the journal's most-downloaded articles (*e.g.*, 2013, 2015, 2017).

5. My research has been sponsored by public agencies including NIH, NSF for over \$16 million, with over \$2 million directly supporting my work as principal investigator ("PI") or Co-PI. I also collaborated with industrial sponsors on various projects focusing on bioimpedance-based diagnostics.

6. I have received numerous awards in research and teaching, including the University of Utah's 2023 Rising Star Award, the President's Research Initiative Award in 2014 and 2016 in the American Association of Neuromuscular & Electrodiagnostic Medicine, and the 2014 Martin Black Prize for Best Paper in Physiological Measurement in 2013.

7. I am the inventor or co-inventor of eight patent application series that were filed in the U.S. and other jurisdictions, which covering a broad range of technology, including bioimpedance and electrical measurements, wearable and non-invasive monitoring, and medical diagnostics.

8. I have served as a peer reviewer for multiple prestigious funding agencies, including the National Science Foundation (NSF) for the Directorate for Engineering, Emerging Frontiers and Multidisciplinary Activities (2024) and the Electrical, Communications and Cyber Systems (ECCS) division (2023).

Additionally, I have reviewed grant proposals for the Estonian Research Council (2020), European Research Council ERC (2020), and Prinses Beatrix Spierfonds (Netherlands, 2019). My extensive experience evaluating cutting-edge research proposals demonstrates my recognized expertise in evaluating technologies in engineering and biomedical fields.

9. I hold key editorial and organizational roles. I currently serve on the Editorial Boards of two flagship IEEE journals, the Open Journal of Engineering in Medicine and Biology (OJEMB) and the Journal of Electromagnetics, RF and Microwaves in Medicine and Biology (J-ERM). Within the IEEE, I serve as a Member-at-Large of the Technical Committee on Biomedical Signal Processing. I was also an Associate Editor for Wiley's International Journal of Circuit Theory & Applications (2020–2021), Physiological Measurement (since 2016).

10. I hold memberships in prestigious societies, including the American Academy of Neurology, the American Association of Neuromuscular & Electrodiagnostic Medicine, and the International Society for Electrical Bio-Impedance. I regularly peer-review for high-impact journals such as Nature Scientific Reports, IEEE Transactions on Biomedical Engineering, and Medical Engineering & Physics. These roles reflect my commitment to fostering interdisciplinary collaboration and translational research at the intersection of engineering and medicine.

11. I also possess extensive industrial experience in translating biomedical technologies from research to commercialization. I co-founded Haystack Diagnostics, Inc. in 2018 and currently serve as Chief Scientific Officer at HemodynamiQ and Chief Scientific Advisor at First Capital Ventures, LLC. Additionally, I have served as a consultant or advisor to multiple medical technology companies including Texas Instruments, Inc., Impedimed, Inc., and Tula Health, Inc. This combination of executive leadership, entrepreneurial experience, and ongoing industry consultation demonstrates my practical understanding of the patent landscape and technology commercialization in biomedical engineering.

12. I have been retained as an expert on behalf of Patent Owner Agilent Technologies, Inc. (“Agilent”). As part of this engagement, I have been asked to provide opinions regarding the subject matter disclosed and claimed by U.S. Patent No. 11, 906,508 (“the ’508 Patent”) (Ex. 1001) and the primary prior art references relied upon by Petitioner Axion BioSystems, Inc. (“Axion”). Those prior art references are U.S. Patent Application No. 2007/0057680 A1 to Jones, et al. (“Jones”) (Ex. 1006) and U.S. Patent No. 7,192,752 to Xu, et al. (“Xu-752”) (Ex. 1005).

13. I have been informed that the ’508 Patent was filed on November 23, 2022 and issued on February 20, 2024. I also understand that the ’508 Patent is a

continuation of a series of patent applications, including U.S. Patent Application No. 12/435,569, filed on May 5, 2009. The '508 Patent claims priority to provisional U.S. Patent Application No. 61/126,533, filed on May 5, 2008.

14. I am not and have never been an employee of Agilent. I also have not consulted with or provided any other services to Agilent in the past. Similarly, I have never been an employee of Axion and I also have not consulted with or provided any other services to Axion in the past. I have been retained by Agilent in this proceeding to provide my independent analysis of the issue raised by the Petition for *inter partes* review of the '508 Patent.

15. I am being compensated at my normal hourly consulting rate of \$500/hour for my work in this proceeding, including studying this matter, preparing this declaration, and providing any cross-examination testimony. My compensation is not contingent upon the outcome of this proceeding or the particular testimony or opinions that I express. I have personal knowledge of the facts stated in the declaration, and I am willing to competently testify to them if and when called to do so.

16. Between now and such time that I may be asked to testify, I expect to continue my review, evaluation, and analysis of evidence presented during this proceeding. I expect to review the declarations and other evidence submitted by Axion's expert(s). I expressly reserve the right to amend or supplement this

declaration, as appropriate, after considering the opinions set forth by Axion's expert(s). I also reserve the right to review and consider that information in further developing or refining my opinions.

II. QUALIFICATIONS AND PROFESSIONAL EXPERIENCE

12. My experience and qualifications are further provided in my *curriculum vitae*, which is submitted with this Declaration. Ex. 2010. My *curriculum vitae* also provides a listing of my publications, conference presentations, chapter books, invited lectures, patents, and other professional activities and services.

13. I graduated with Bachelor of Science degrees in Telecommunication Engineering (2006) and in Electrical Engineering (2007) from TelecomBCN, one of the largest telecommunications engineering schools in Spain. I received a Master's degree in Electrical Engineering in 2008, and completed a Ph.D. in Electrical Engineering in 2012, both from TelecomBCN.

14. I then spent two years as a postdoctoral scholar at TelecomBCN working with Ramon Bragos, Ph.D., from January 2012 to December 2013. The research was about temporal impedance variations of myocardium during the cardiac cycle. I collaborated with Rik Pintelon, Ph.D., at Vrije Universiteit Brussel and Cristian Rojas, Ph.D., at KTH-Royal Institute of Technology as a Visiting Scientist from April 2013 to December 2013. In January 2014, I joined

Beth Israel Deaconess Medical Center, Harvard Medical School, as an Instructor in Neurology focusing on the evaluation of neuromuscular disorders. In July 2020, I was hired as an Assistant Professor at the Department of Electrical and Computer Engineering, University of Utah. Most recently, in January 2025, I became an Associate Professor in the Department of Electrical and Computer Engineering, Richard and Loan Hill Department of Biomedical Engineering, at the University of Illinois Chicago.

III. MATERIALS CONSIDERED AND BASIS FOR TESTIMONY

15. In forming my opinions, I have reviewed the '508 Patent, portions of its file history, and the other materials cited in my declaration. The bases for my opinions include the following: (i) my education in electrical engineering; (ii) my about twenty-five years of experience in electrical engineering, computer engineering, and bioengineering; and (iii) my review of certain documents as cited in my declaration. These documents include:

- a. Petition for Inter Partes Review by Axion BioSciences, Inc.
- b. U.S. Pat. No. 11,906,508 ("the '508 Patent") (Ex. 1001)
- c. Excerpts of the Prosecution History of U.S. Patent No. the '508 Patent (Ex. 1002)
- d. Declaration of Bruce C. Kim, Ph.D. (Ex. 1003)
- e. Curriculum Vitae of Declaration of Bruce C. Kim, Ph.D. (Ex. 1004)

- f. U.S. Patent No. 7,192,752 to Xu, et al. (“Xu-752”) (Ex. 1005)
- g. U.S. Patent Application No. 2007/0057680 A1 to Jones, et al.
 (“Jones”) (Ex. 1006)
- h. U.S. Patent No. 7,459,918 o Jones, et al. (“Jones Patent”) (Ex. 1007)
- i. Statutory Disclaimer of Agilent Technologies, Inc. (Ex. 2001)
- j. Modern Dictionary of Electronics (1999) (excerpts) (Ex. 2006)
- k. The Board’s Decision to institute this IPR
- l. U.S. Patent App. Pub. No. 2008/0043448A1 (“Finnerty”) (Ex. 2014)
- m. U.S. Patent App. Pub. No. 2008/0068790A1 (“Lee”) (Ex. 2015)
- n. U.S. Patent App. Pub. No. 2008/0037218A1 (“Sharma”) (Ex. 2016)
- o. U.S. Patent App. Pub. No. 2008/0298014A1 (“Franco”) (Ex. 2017)
- p. U.S. Patent App. Pub. No. 2008/0257594A1 (“Engblom”) (Ex. 2018)
- q. U.S. Patent App. Pub. No. 2008/0304223A1 (“Franz”) (Ex. 2019)

The above-referenced materials are in addition to any other materials referenced directly or indirectly in this Declaration.

IV. LEGAL PRINCIPLES

A. Person of Ordinary Skill in the Art

16. I understand that a patent claim is evaluated from the perspective of a “person of ordinary skill in the art” (“POSA”), which I understand is a hypothetical person considered to have the skill level and knowledge of a particular field related

to an alleged invention claimed in a patent. I further understand that this hypothetical skilled artisan is presumed to have before him or her all of the relevant prior art. I understand that this “hypothetical person” can be more than one person or a team of people of different disciplines. The discussions in this declaration are intended to convey the state of the art and the knowledge of a POSA generally prior to the earliest effective filing date of the patent application that issued as the respective ’508 Patent, which I understand is May 5, 2008, based on the filing date of the provisional application to which the ’508 Patent claims priority.

17. I understand that Axion contends that a person of ordinary skill in the art (“POSA”) as of May 2009 “would have had a B.S. in electrical/mechanical/ biomedical engineering or biological science, or a related field, and approximately 2 years of relevant experience or equivalent study in systems and methods for bioanalysis of cells.” Pet. 14 (citing Ex. 1003 ¶¶ 23–25).

18. I further understand that in its Institution Decision the Board found that Axion’s description of the level of ordinary skill in the art to be sufficiently supported by the record and applied it for purposes of that decision. DI at 7.

19. In this context, I have been asked to also define the level of a POSA with regard to this proceeding. In defining the level of a POSA, I have been informed that a list of non-exhaustive factors to consider include: (1) the type of

problems encountered in the art; (2) the prior art solutions to those problems; (3) the rapidity with which inventions are made; (4) the sophistication of the technology; and (5) the education level of active workers in the field. Based on the foregoing, in my opinion Axion's definition is reasonable, namely, a POSA as of the time of the invention "would have had a B.S. in electrical/mechanical/ biomedical engineering or biological science, or a related field, and approximately 2 years of relevant experience or equivalent study in systems and methods for bioanalysis of cells." As of the time of the invention, I was at least at the level of a POSA with respect to the '508 Patent.

20. All of my opinions set forth herein are provided from the perspective of a POSA at the time of the invention of the '508 Patent.

B. Claim Construction

21. I understand that the first step in analyzing a patent claim begins with an analysis of the wording of the claim itself, also referred to as "claim construction."

22. I understand that claim terms in an *inter partes* review should be accorded their ordinary and customary meaning as understood by a POSA at the time of the invention, in light of the patent specification and the prosecution history pertaining to the patent. I further understand that when the specification expressly defines terms used in the claims or when it defines terms by implication,

it acts as a dictionary.

23. I understand that the specification of the '508 Patent includes a “Definitions” section, which expressly defines numerous terms. Ex. 1001, Cols. 9:35 – 16:14. These definitions provided in the '508 Patent provide the POSA with essential understandings of the meanings of the claim terms.

24. As set forth herein, I apply these principles to my discussion below of the '508 Patent's claims with respect to the “millisecond time resolution” of Claims 1-8 and 11-15.

V. OVERVIEW OF THE TECHNOLOGY OF THE '508 PATENT

25. The '508 Patent, issued on February 20, 2024, is directed to impedance-based cellular analysis systems and methods for monitoring excitation-contraction coupling and excitable cells. Ex. 1001, Col. 1:28-32. Although impedance-based cellular analysis had been known in 2008, the '508 Patent was the first to describe an impedance-based cellular analysis with “millisecond time resolution”, which was accomplished when an impedance analyzer measures two consecutive impedances of multiple wells simultaneously or nearly simultaneously. The system further includes “a software program that controls the electronic circuitry and records and analyzes data obtained from the impedance analyzer.” *Id.* at Col. 3:11-13. This new system is particularly helpful to monitor fast cellular activities, such as excitation and contraction coupling of

cardiomyocytes, cardio safety profiling/analysis for drugs or drug candidates, functional studies of cardiomyocytes derived from stem cells, cardio disease modelling by gene modification of cardiomyocyte, and physiological and disease processes of muscle cells in a high throughput manner.

VI. STATUTORY DISCLAIMER

26. I understand that on December 20, 2024, Agilent filed a statutory disclaimer of Claims 9, 10, and 23-30 of the '508 Patent. Ex. 2001. I understand that the statutory disclaimer effectively cancels the above listed claims from the '508 Patent and that those claims were not considered by the Board in deciding to grant Axion's petition.

27. I further understand that on June 19, 2025, Agilent filed a second statutory disclaimer of Claims 16-22 of the '508 Patent. Ex.2020. I understand that the statutory disclaimer effectively cancels the above listed claims from the '508 Patent and that those claims should not be considered by the Board in making the final decision.

VII. THE TERM "MILLISECOND TIME RESOLUTION"

28. I have reviewed the claims and specification of the '508 Patent in order to determine the ordinary and customary meaning of the claims in view of the patent's specification.

29. The specification of the '508 Patent includes a "Definitions"

section, which defines numerous terms including “millisecond time resolution.”

Ex. 1001, Cols. 9:35 – 16:14. The specification also explains that “the definition set forth in this section prevails over the definition that is incorporated herein by reference.” *Id.*, Col. 9:45-47.

30. Specifically, the “Definitions” section of the ’508 Patent explicitly defines the term “millisecond time resolution” as follows:

As used herein, “impedance measurement at millisecond time resolution” refers to the ability to perform a series of at least two consecutive impedance measurements within milliseconds of one another for each and every well of the system where each well is associated with an electrode array for impedance measurement. In each instance the time between two consecutive impedance measurements are less than 300 milliseconds from one another.

Preferably, consecutive impedance measurements are less than 200 milliseconds from one another. More preferably impedance measurements are less than 100 milliseconds from one another. For example, the time between two consecutive impedance measurements are 40 milliseconds from one another for each and every well of the system. To be clear, that is to say, in a time period of 40 milliseconds, the system has the ability to measure two impedance data points for each and every well of the system.

Ex. 1001, Col. 10:8-24 (emphasis added).

31. Under this definition, the term “millisecond time resolution” refers to the ability to perform at least two consecutive impedance measurements for

each and every well being evaluated in the claimed apparatus or system can be performed in less than 300 milliseconds from one another. As discussed further below, in view of the entirety of the '508 Patent's specification, and for purposes of this IPR proceeding, I will use 500 milliseconds rather than 300 milliseconds.

32. This definition is consistent with other disclosures in the specification of the '508 Patent:

In embodiments where the device includes multiple wells, the impedance analyzer has the capability to allow impedance measurements for each and every well at millisecond time resolution. That is to say, for a selected time period, the impedance data for each and every well of the system is measured at millisecond time resolution. Further, when groups of wells are monitored, the groups are monitored at millisecond time resolution.

Id., Col. 3:24-32.

Throughout the present application where the device includes multiple wells each of which is associated with an electrode array, millisecond time resolution refers to that for any selected time period, the impedance measurement for each and every well can be performed with two consecutive measurements separated with millisecond resolution. Further, when groups of wells, such as subsets of all wells of a device, are monitored a group of wells may be monitored using millisecond time resolution.

Id., Cols. 3:65 – 4:6.

For example, if the system comprises a device having 96 wells, the system hardware and software should be capable of, for a given time period, measuring the impedances of all 96 wells with millisecond time resolution between two adjacent or consecutive impedance measurement points for each and every well. Thus, comparing two impedance analyzers, one for impedance measurement of 96 wells with millisecond resolution and another for impedance measurement of a single well with millisecond time resolution, the one for 96 well measurement is effectively 96-times faster than one for a single well measurement since it is required to have a capability for performing impedance measurement for all 96 wells with millisecond time resolution.

Id., Col. 24:22-35.

33. I understand that in the Institution Decision, the Board noted that while the '508 Patent expressly defines "millisecond time resolution" using the "less than 300 milliseconds" formulation, several other instances in the patent (including now-disclaimed Claims 9 and 10) state "less than 500 milliseconds". DI at 10-11, 25. In light of the "1.5 second update period" disclosure in Jones, it is my opinion that the distinction between 300 milliseconds and 500 milliseconds does exist, but it is immaterial to the dispute in this IPR. Ex. 1006 ¶ [0030]. Furthermore, I understand that, for purposes of this IPR, Agilent has proposed that the term "millisecond time resolution" be construed to mean the time between two consecutive impedance measurements for each and every

well being evaluated in the claimed apparatus or system, which can be performed in less than 500 milliseconds from one another. For purposes of this IPR proceeding, I will adopt 500 milliseconds rather than 300 milliseconds.

34. It is my opinion that Axion relies on an incorrect understanding of the claim term “millisecond time resolution” to support its Ground 2 challenge. Axion appears to solely rely on Jones’ Paragraph [0030] to support the “millisecond time resolution”, which was the only time in Jones that mentions millisecond. Paragraph [0030] states in its entirety:

Each well is subject to a stepped sweep (a series of single frequency bursts-one burst for each selected frequency). The bursts consist of an integral number of cycles. In one embodiment, the number of cycles is typically 15. The number of cycles for additional embodiments are chosen to be sufficient for well and gain multiplexer switching transients to settle and to obtain the necessary number of sample points. From preliminary modeling and testing, no more than 68.2 ms per well for all frequencies is required to obtain sufficient samples. For an embodiment in which a 96 well plate with 12 wells per row plus four reference network channels, 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.

Ex. 1006 ¶ [0030].

35. The disclosed 68.2 milliseconds in Jones is the time required to

obtain sufficient samples per well, and the suggested 1,091 millisecond measurement period is exactly the total measurement time of 12 wells and four reference channels, that is 16 times 68.2 milliseconds, which is consistent with Jones' teaching of multiplexing 12 rows plus 4 reference channels when they are measured one after another (i.e., making one measurement at a time).

Accordingly, Jones uses a multiplexer and measurement circuitry to measure each well per row on the plate sequentially (one well at a time) but not simultaneously, which results in a 1.5 second update period. This update period is at least three times slower than the claimed 500ms or less "millisecond time resolution" in the '508 Patent.

36. In its Petition, Axion erroneously treats the 68.2 milliseconds as a benchmark for calculating the time between consecutive measurements of all of the wells being evaluated in the '508 patent. Axion incorrectly asserts that "[t]he disclosure in Jones also describes taking first and second measurements of impedance of a single well of a 96-well plate milliseconds apart as part of the stepped frequency sweep that is completed for each well in 'no more than 68.2 ms per well.' EX1006, ¶[0030]." Pet. at 35. It is clear that Axion misunderstands that the 68.2 ms discussed by Jones is the time required to measure a single well, not the total measurement time necessary to perform a consecutive measurement of that well. Indeed, in the very next sentence, Jones

explains that the time between consecutive measurements of a given well is 1.5 seconds. Ex. 1006 ¶ [0030].

37. Finally, Axion asserts, again incorrectly, that “for a multiwell 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”.

38. In my opinion, Axion relies on an incorrect understanding of the claim term “millisecond time resolution” to support its Ground 2 challenge. It is my understanding that Jones does not teach or suggest the “millisecond time resolution” limitation, which requires that the system or apparatus must be capable of performing at least two consecutive impedance measurements within a time of no more than 500 milliseconds across all of the wells being evaluated on a well plate.

39. Jones nowhere mentions or suggests of calculating impedance values of two or more wells in parallel, or an impedance analyzer that measures

the impedances of multiple wells simultaneously or nearly simultaneously. The only discussions of “processing” impedance data (*i.e.*, the voltages and currents from the sensors) are in the context of using a multiplexer (or electronic switch) for switching the impedance measurement circuitry from one well to another well to enable impedance measurement to be taken in series (or serial) one well at a time:

The ZMS utilizes a novel combination of parallel impedance measurement channels and the multiplexing of impedance measurement channels for interconnecting multiple microtiter plate sensors and reference impedance networks to the channels

* * *

[E]ach row of sensors on a microtiter plate is addressed by measurement circuitry (in the form of analog signal conditioning circuits, multiplexing circuits, analog digital converters, and digital signal processors) on a single daughter board.

* * *

Each daughter board has multiplexing circuitry allowing one or more measurement channels to address the sensors for each well in the row.

* * *

For an embodiment in which a 96 well plate with 12 wells per row plus four reference network channels, 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.

Ex. 1006 ¶¶ [0003], [0012], [0030] (emphases added).

40. Jones' Paragraph [0030] describes a system that requires a measurement time for a single well to be “no more than 68.2 ms *per well*,” to achieve a “target 1.5 second update period.” Ex. 1006 ¶ [0030]. Thus, Jones teaches that it requires 1.5 seconds between two measurements of each well (the “update period”): 12 wells plus the 4 reference channels on a daughter board measured sequentially (in series, that is one after the other), with an additional 0.409 seconds for “multiplexer switching and signal settling” ($0.0682 \text{ seconds} \times (12 + 4) + 0.409 \text{ seconds} = 1.5 \text{ seconds}$). *Id.* This further teaches that the 12 wells in a row (with 4 additional channels) are measured one at a time and one after another, *i.e.*, in series, such that a measurement time of 68.2 ms per well provides a total measurement time of $(12 + 4) \times 68.2 \text{ ms} = 1,091 \text{ milliseconds}$. *Id.* Because the 12 wells in the row are measured in series, an additional 0.409 seconds is included for “multiplexer switching and signal settling.” *Id.* The total of the measurement time plus the “multiplexer switching and signal settling” time is the 1.5 seconds for the “target update period.” Accordingly, the system disclosed in Jones operates on a time resolution on the scale of seconds, which is three times slower than the less than 500 millisecond time resolution described and claimed in the '508 Patent.

41. Jones' target 1.5 second throughput requirement is consistent with the

“2 or 10 second update rate” specified for the commercial CellKey impedance measurement system introduced on September 8, 2005 by MDS Sciex, who I understand is the assignee of the Jones application (filed on September 9, 2005):

Update rate 96-well	2 or 10 second update rate
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Ex. 2011 at 6 (MDS Sciex CellKey Brochure (Instrument Specifications)); Ex. 1006 at 1 (73); Ex. 2012 (CellKey Specifications (2007)); Ex. 2013 (CellKey Press Release (2005)).

42. I note that the times for the “multiplexer switching and signal settling” in the above illustration would be interspersed throughout the entire 1.5 second update period, with electrical transients occurring after each multiplexer switching operation between wells and reference channels within a row in the microtiter plate. It is my opinion that Axion misinterpreted the “millisecond time resolution” limitation to simply mean the time required to measure the impedance of a single well, rather than the time required between two consecutive impedance measurements of each and every well of the claimed apparatus or system being evaluated.

43. In contrast to Jones, the '508 Patent explains this difference in measurement speed with an illustrative example:

Thus, comparing two impedance analyzers, one for impedance

measurement of 96 wells with millisecond resolution and another for impedance measurement of a single well with millisecond time resolution, the one for 96 well measurement is effectively 96-times faster than one for a single well measurement since it is required to have a capability for performing impedance measurement for all 96 wells with millisecond time resolution.

Ex. 1001, Col. 24:27-35.

44. As its specification describes, the '508 Patent is directed to “systems and methods for monitoring excitation-contraction coupling and excitable cells using impedance based systems with millisecond time resolution.” Ex. 1001, Col. 1:28-32. Thus, the invention claimed in the '508 Patent “fill[s] a major technological gap in monitoring of excitation-contraction coupling and excitable cells, such as cardiomyocytes, in vitro[,] . . . in part, [by] the development of an impedance-based system and monitoring method that employs millisecond time resolution.” *Id.*, Col. 16:19-24; *see also id.*, Col. 3:48-54 (“[M]illisecond time resolution enhances measurement such that excitation-contraction coupling of excitable cells may be effectively monitored. In some embodiments the excitation cycle is a beating cycle, such as a beating cycle of a cardiomyocyte.”), Col. 30:38-41 (“[T]he development of millisecond time resolution permits impedance monitoring of the cardiomyocyte beating cycle as well as fluctuations, even minor alterations, in response to external stimuli.”). In my opinion, these statements are

accurate.

45. For example, for cardiomyocytes, “[a] beating cycle may be as short as between 100 and 200 milliseconds, translating to a beating rate of 600 to 300 beats per minute.” *Id.*, Col. 10:44-46. Because of the important applications repeatedly discussed, the ’508 Patent focuses on time resolutions between two measurements of “less than 500 milliseconds” as the minimum, but the system in the ’508 Patent is capable of performing two consecutive measurements with even shorter time:

The method has particular utility with cells that are known or suspected to be capable of or undergo excitation-contraction coupling, such as cardiomyocytes. The method may also be useful for monitoring neurological cells or neurological systems. Impedance measurements may be performed in millisecond time resolution. In some embodiments, two consecutive impedance measurements for each and every well of the system are performed less than 300 milliseconds apart.

Id., Col. 4:51-59; *see id.*, Col. 47:15 (“millisecond time resolution”) (Cl. 1), Col. 47:54 (“less than 100 milliseconds”) (Cl. 11), Col. 47:57 (“less than 40 milliseconds”) (Cl. 12), Col. 47:59 (“less than 20 milliseconds”) (Cl. 13), Col. 47:62 (“less than 5 milliseconds”) (Cl. 14). In my opinion, these statements are accurate.

46. The specification of the ’508 Patent explains that these kinds of

applications may require time resolutions much less than 300 milliseconds:

With millisecond time resolution for impedance measurement, it becomes possible to resolve individual beating cycles of cardiomyocytes cultured on electrodes. Whilst theoretically one needs at least two data points for each beating cycle, in practice more than 2 data points are needed for each beating cycle. For example, if cells have a beating rate of 60 beats per minute, i.e[.], one beat per second. It would be preferred to have a time resolution of at least 200 milliseconds so that each beating cycle consists of 5 data points. More preferably, the measurement time resolution is 100 milliseconds. Still more preferably, the time resolution is 50 milliseconds or less.

Id., Col. 25:33-44. In my opinion, these statements are accurate.

47. Additionally, the '508 Patent explains why then-existing systems that used “seconds” time resolution between consecutive impedance measurements (like Jones’ “target 1.5 second update period”) would be incapable of accomplishing the objectives of the invention (emphasis added):

Millisecond time resolution of impedance-based devices provides a significant technical step over traditional impedance measuring devices, which are typically limited to **second** or minute **resolution**.

* * *

Without millisecond time resolution, it would not be possible to perform detailed analysis of the beating cycle of the excitable cells. For example, for cardiomyocytes, if the impedance is measured at **seconds time-resolution** such as a ten-second or **even one-second**

resolution, it would not be possible to observe beating of the cardiomyocytes or resolve a beating cycle of the cardiomyocytes with an impedance measurement. The cardiomyocytes-beating-resulted impedance change would be shown as “noise” on the impedance curves measured at **seconds** or minutes **time-resolution**.

Id., Cols. 24:11-14, 16:40-58. In my opinion, these statements are accurate. Thus, the impedance measuring system disclosed in Jones with the 1.5 seconds “update period” would not be able to effectively perform the analysis of the excitable cells repeatedly discussed and emphasized in the ’508 Patent.

48. Jones is directed to the physical arrangement of its system, with the goal of improving “internal correction of impedance measurement drift, maximized measurement accuracy, and minimized system size.” Ex. 1006, Abstract. Jones does not describe or suggest any particular applications for its system, including the types of cells to be monitored or their particular nature (such as excitable cells or cardiomyocytes). Nor does Jones disclose millisecond time resolution or include any discussion about improving measurement time resolution.

49. It is my understanding that Jones does not mention any particular applications for its system, including the types of cells to be monitored or their particular nature (such as excitable cells or cardiomyocytes). And Jones does not disclose millisecond time resolution or include any discussion about improving measurement time resolution. Instead, as discussed previously, Jones is directed to

the physical arrangement of its system, with the goal of improving “internal correction of impedance measurement drift, maximized measurement accuracy, and minimized system size.” Ex. 1006, Abstr. Additionally, Jones discloses hardware “parallelism” to achieve its goal of increased measurement accuracy and stabilization:

[T]he ZMS employs [hardware] parallelism to obtain the required throughput at the repeatability required and incorporates novel calibration, self-check, and in-run compensation schemes as well as internal temperature control to ensure increased measurement accuracy and stabilization against thermal drift.

Id. ¶ [0003].

50. The ’508 Patent’s described and claimed “millisecond time resolution” provides a substantial improvement in cellular impedance measurements, particularly with respect to applications such as excitation-contraction coupling and excitable cells.

51. Additionally, I understand that the Board expressed “some initial concerns we have regarding Petitioner’s showing for the ‘millisecond time resolution’ limitation” by relying on the calculation in Axion’s expert report (Ex. 1003). DI. at 24-25. The Board elaborated that “Dr. Kim’s examples **modify multiple aspects of Jones’s 96-well embodiment**, *i.e.*, 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”, however, “the reasoning for those changes is not explained sufficiently in the Petition.” DI. at 23-24.

52. 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. A POSA would understand that Jones teaches that its impedance measurement system has a “target 1.5 second update period”, which is consistent with the update rate of impedance measurement systems in that era (namely, a few seconds). Jones nowhere teaches or even suggests that its system could operate faster than its specified update period, nor does Jones anywhere teach or even suggest that there is a need or desire to increase that rate.

53. As mentioned previously, Jones does not discuss any types of cells to be analyzed by its system, and thus *increasing* throughput is nowhere contemplated. Jones’ objective was to condense the existing larger format systems into a smaller form factor, consistent with the general trends in the industry, while maintaining the specifications of those systems for such parameters as accuracy, repeatability, and throughput.

54. In summary, it is my opinion that the 1.5 second update period disclosed in Jones would be unable to effectively perform the analysis of the excitable cells repeatedly discussed and emphasized in the '508 Patent. It is my opinion that nowhere in Jones discusses any objective of measuring impedance in millisecond time resolution, which was not the purpose of Jones. And Jones does not discuss the types of cells that are to be measured by the disclosed system. Thus, even if Axion's argument that a POSA would have been motivated to develop an impedance system capable of millisecond time resolution, a POSA would not look to combine Xu-752 with Jones because Jones does not teach an impedance system capable of millisecond time resolution, or even suggest any solution or reason to increase the "target 1.5 second time period" of Jones' disclosed system. The combination of Xu-752 and Jones would not make claims in the '508 Patent obvious.

VIII. JONES' OBJECTIVE TO STABILIZE THE SYSTEM FROM THERMAL DRIFT IS CONSISTENT WITH PRIOR ART

55. The closely packed parallel daughter boards in Jones were arranged to achieve a compact form factor and temperature control. In my opinion, the focus of Jones is to control thermal transients and maintain measurement accuracy, when condensing an impedance measuring system into a compact form factor (including by using parallel mezzanine cards or "daughter boards"). Jones nowhere discusses any objective of measuring

impedance in millisecond time resolution. (“the ZMS (Impedance Measurement System”) employs parallelism to obtain ... as well as **internal temperature control** to ensure increased measurement accuracy and **stabilization against thermal drift.**”). Ex. 1006 at [0003]. Jones explains that the purpose of its systems’ parallel physical arrangement is to maintain specified accuracy and repeatability within a smaller and denser form factor (because the daughter boards are arranged physically in parallel next to each other, the overall system dimensions are reduced):

Electrical performance dictates that the daughter board assembly be closely coupled to the top contact board and that the circuitry be kept as tightly arranged as possible.

* * *

This physical arrangement and electrical configuration maximizes the accuracy of the impedance measurements by minimizing the electrical path length and stray impedances associated with connecting the microtiter plate sensor to the measurement circuit. The minimized path length also optimizes phase and gain tracking, and maximizes the immunity to noise.

The physical configuration minimizes the number of needed mechanical supports and eliminates key thermal expansion problems

associated with other designs. The configuration minimizes the size of the Impedance Measurement System thereby allowing more efficient internal packaging and thermal stabilization of the electronic components (due to reduced convection). The minimized path length also optimizes phase and gain tracking, and maximizes the immunity to noise.

Ex. 1006 ¶¶ [0021], [0023]-[0024].

56. In my opinion, If a POSA would have wanted to develop an impedance system that would be capable of millisecond time resolution as claimed in the '508 Patent, the POSA would not look to Jones because Jones does not teach an impedance system capable of millisecond time resolution, or even suggest any solution or reason to increase the target 1.5 second time resolution of Jones' disclosed system. Instead, Jones focuses on controlling thermal transients and maintain measurement accuracy within the compact form. The daughter boards are arranged physically parallel next to each other, the overall system dimensions are reduced. On the other hand, Jones does not disclose or suggest improving the speed of making impedance measurements, which leads to an "increased throughput".

57. In light of the discussion above, with regard to the phrase in Jones stating, "to obtain the **required throughput** at the repeatability

required”, Jones teaches nothing about “improving” or “increasing” throughput, but only “increased measurement accuracy,” which is different from what was claimed in the ’508 Patent:

58. Therefore, it is my opinion that, in the context of Jones, the “required throughput” is clearly stated: “the target 1.5 second update period.” Ex. 1006 ¶ [0030]. In my opinion, all of Jones’ claims only use “parallel” and “perpendicular” to recite the physical arrangement of the components in the system. Jones doesn’t discuss any ability to have an impedance analyzer measure the impedances of multiple wells simultaneously or nearly simultaneously. In other words, Jones sticks to “one-to-one” measurement, not “one-to-multiple” as claimed in the ’508 Patent. Furthermore, Jones only discloses making serial impedance measurements on each daughter board, and does not disclose or suggest “an impedance analyzer” which measures “a first plurality of cell-substrate impedances at a first time and a second plurality of cell-substrate impedances at a second time.”

59. This purpose to control heat in a compact system is consistent with contemporaneous patent applications discussing the growing adoption of the PCI Mezzanine Card (PMC) standard to achieve heat dissipation and temperature control. Jones’ express focus on a compact form factor and

temperature control in conjunction with closely packed parallel daughter boards is consistent with contemporaneous patent applications discussing the growing adoption of, for example, the PCI Mezzanine Card (PMC) standard and the PCI eXtensions for Instrumentation (PXI) standard to achieve those competing goals.

60. In Finnerty, Ex. 2014, heat dissipation is an area of concern when using mezzanine cards:

One solution to this problem is the use of a supplemental card portion called a ‘mezzanine’ card (sometimes referred to as a ‘daughter’ card) that is mounted to the main circuit card (referred to generically as the carrier card) in order to provide one or more additional connectors and additional I/O pins.

* * *

The present invention provides the advantages of increasing the I/O flexibility of a carrier card such as a PMC, provides acceptable heat dissipation within a small physical form factor

Id. ¶¶ [0003], [0008].

61. In Lee, Ex. 2015, physically paralleled Advanced Mezzanine Card (AdvancedMC) were utilized to increase heat dissipation when the size is reduced:

To increase heat dissipation further, fans may be used to provide forced convection within a computer or electronic system or to provide impinging cooling directly on a heat sink.

* * *

Developments in computer hardware have also resulted in space constraints, particularly in small form factors and modular computer platforms, such as Advanced Telecommunications Computing Architecture (AdvancedTCA), Advanced Mezzanine Card (AdvancedMC) and Compact Peripheral Component Interconnect (CompactPCI).

Id. ¶¶ [0002], [0003].

62. Sharma, Ex. 2016, contains a similar discussion:

Where the unit chassis comprises a mechanically and electrically interconnected structure having the smallest form factor compliant with the MicroTCA standard but still capable of delivering scalable mechanical, electrical and environmental functionality to support at least one AdvancedTCA module.

* * *

[a] second paired cooling unit proximate an exhaust vent operative to push the air out of the enclosure so as to deliver the standards-defined

cooling performance in a compact, cost-effective package that maximizes the volume of the enclosure available for housing modules.

Id. Cols. 5:56-61, 7:45-49.

63. In Franco, Ex. 2017, two parallel channels for hot swapping and cooperate in a push-pull cooling arrangement were disclosed:

A plurality of combined card guides is provided to align connectors on mid-size AdvancedMCs with corresponding connectors on the backplane. A combined card guide has a height adapted to fit between an inner surface of the chassis cover and an inner surface of the chassis bottom and is formed with two parallel channels along a length of the guide to provide support for two AdvancedMCs or similar electronic modules, one above the other.

* * *

The first and second cooling units are adapted for hot swapping and cooperate in a push-pull cooling arrangement to cool the interior of the modular electronic enclosure.

Id. Cols. 3:54-61, 4:9-11.

64. In Engblom, Ex. 2018, the object of the invention was to enable a compact design of printed board assemblies:

The features of the present invention are particularly advantageous

where a compact design is wanted and there are restraints on the format.

* * *

A cooling unit #16 is provided for controlling the thermal conditions of the components of the MicroTCA system 1.

Id. ¶¶ [0024], [0029].

65. Franz, Ex. 2019, the expansion card was inserted or installed parallel to the system board of the server:

Expansion cards for blade servers may have a mezzanine design, in which the expansion card is inserted or installed parallel to the system board of the server.

* * *

Installing the mezzanine cards at different heights in a staggered configuration provides for the mezzanine cards to have the smallest footprint on the system board, yet allow space for all necessary components, heat sinks, and air flow for cooling.

Id. ¶¶ [0002], [0013].

66. The above cited prior art reference to Jones share common features with Jones for the physically paralleled arrangement of daughterboards. As explicitly stated in Jones, the parallel arrangement was

to achieve “internal temperature control to ensure increased measurement accuracy and stabilization against thermal drift.” Ex. 1006 at [0003]. In contrast, Jones did not make any claim about increase the measurement capacity as claimed in the '508 Patent.

I declare under penalty of perjury under the law of the United States that all statements made herein of my own knowledge are true and that all statements made on information and believe are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.



Dated: __June 19th__, 2025

Benjamin Sanchez Terrones, Ph.D.