UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SIEMENS HEALTHCARE
DIAGNOSTICS INC.,
Petitioner,

v.

RADIOMETER MEDICAL APS,
Patent Owner.

Case IPR2018-00311
Patent 8,728,288

PETITION FOR *INTER PARTES* REVIEW

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LIST OF EXHIBITS

Exhibit No.	Description
1001	U.S. Patent No. 8,728,288 (filed Apr. 24, 2008) (“288 patent”)
1002	Prosecution history for the 288 patent (“288 prosecution history”)
1003	U.S. Patent No. 5,916,425 (filed May 16, 1996) (“Leader”)
1004	U.S. Patent No. 6,123,820 (filed Jun. 5, 1998) (“Bergkuist”)
1005	Joseph Wang et al., *Coated Amperometric Electrode Arrays for Multicomponent Analysis*, 62 Anal. Chem. 1924-27 (1990) (“Wang”)
1006	U.S. Patent No. 6,652,810 (filed Nov. 28, 2000) (“Ziegler”)
1007	U.S. Patent Publication No. 2004/0043477 (published Mar. 4, 2004) (“Schibli”)
1008	U.S. Patent Publication No. 2004/0189311 (published Sep. 30, 2004) (“Glezer”)
1009	U.S. Patent No. 6,207,369 (filed Sep. 17, 1996) (“Wohlstadter”)
1010	Pranitis et al., *Potentiometric Ion-, Gas-, and Bio-Selective Membrane Electrodes*, 23 Critical Reviews in Analytical Chemistry 3, 163-186 (1992) (“Pranitis” or “Meyerhoff”)
1011	Rees et al., *Voltammetry Under High Mass Transport Conditions. The High Speed Channel Electrode and Heterogenous Kinetics*, 99 J. Phys. Chem. 40, 14813-18 (1995) (“Rees” or “Compton”)
1012	Strike et al., *Electrochemical Techniques for the Modification of Microelectrodes*, 10 Biosensors and Bioelectronics 1-2, 61-66 (1995) (“Strike”)
1013	Lauks, *Microfabricated Biosensors and Microanalytical Systems for Blood Analysis*, 31 Chem. Res. 5, 317-24 (1998) (“Lauks”)

1020	December 20, 2017 Declaration of Richard M. Crooks, Ph.D. (“Crooks Decl.”)

I. Introduction

Pursuant to 35 U.S.C. §§ 311-319 and 37 C.F.R. § 42, Siemens Healthcare Diagnostics Inc. ("Siemens" or "Petitioner") hereby petitions for *inter partes* review of claims 1-13 (the "Challenged Claims") of U.S. Patent No. 8,728,288 (the "288 patent") (Ex. 1001), currently assigned to Radiometer Medical ApS ("Radiometer" or "Patent Owner").

The 288 patent discloses and claims a sensor assembly applicable for electrochemically detecting various analytes in blood. The 288 patent relies upon — and alleges to improve upon — a prior art patent to Leader. Leader, in turn, disclosed a linear flow cell with a series of electrochemical sensors disposed along a wiring substrate forming a surface of the flow cell. The inventors of Leader advanced the field by miniaturizing the sensors, allowing more sensors to fit in a smaller area and beneficially reducing blood sample sizes. The 288 patent makes use of the same wiring substrates and sensors as Leader, but purports to further innovate by placing the sensors along both surfaces of the flow cell in an opposing configuration, allowing for a shorter flow cell and, again, reduced blood sample sizes.

As will be demonstrated in great detail below, the prior art shows that ordinarily skilled artisans knew that reducing sample volume was an important goal; knew that placing sensors along both surfaces of a flow cell was a way to achieve that goal; and knew exactly how to modify Leader to provide for a flow cell with sensor-lined wiring substrates on either side. The key prior art disclosures that prove that the 288 patent would have been obvious derive from prior art that the examiner lacked: Wang (Ex. 1005); Ziegler (Ex. 1006); Schibli (Ex. 1007); and Glezer (Ex. 1008). And the testimony of Dr. Crooks, a renowned expert in electrochemistry, explains what a person of ordinary skill in the art would have learned from these references, and how she would have applied those teachings to the problems in the field. The claims of the 288 patent represent nothing more than the routine work of a person of ordinary skill in the art, applying a known solution to a known problem by combining known components to reach predictable results.

Siemens therefore respectfully requests review and cancellation of the Challenged Claims because, as shown below, and in light of the supporting Declaration of Dr. Crooks, there is more than a reasonable likelihood that the Challenged Claims are unpatentable under 35 U.S.C. § 103(a).

II. Mandatory Notices

A. Rule 42.8(b)(1) – Real Party-In-Interest

Petitioner Siemens Healthcare Diagnostics Inc. is a real party-in-interest. Siemens Healthcare Diagnostics Inc.'s corporate parents may also be considered real parties-in-interest. Those entities are Siemens Medical Solutions USA, Inc., Siemens Healthcare GmbH, and Siemens AG.

B. Rule 42.8(b)(2) – Related Matters

Petitioner is unaware of any judicial or administrative matters that would affect, or be affected by, a decision in this proceeding.

C. Lead and Back-Up Counsel and Service Information

Petitioner submits herewith a power of attorney and designates the following counsel pursuant to 37 C.F.R. §§ 42.8(b)(3), 42.10(a), and §42.10(b). Service information is also shown in this chart:

Lead Counsel	Back-Up Counsel
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Petitioner agrees to accept service by email.

III. Payment of Fees

The undersigned authorizes the Office to charge $24,000 to Deposit Account No. 233050 for review of the thirteen challenged claims ($9,000 under 37 C.F.R. § 42.15(a)(1) and (3), and $15,000 under 37 C.F.R. § 42.15(a)(2) and (4) (including, if applicable, the 2018 fee increase per 82 Fed. Reg. 52780, 52807 (Nov. 14, 2017)). The undersigned further authorizes the Office to charge this Deposit Account for any additional fees that might be due in connection with this Petition.

IV. Requirements for *Inter Partes* Review

A. Rule 42.104(a) – Grounds for Standing

Petitioner certifies that the 288 patent is available for, and Petitioner is not barred or estopped from requesting, *inter partes* review of any claim of the 288 patent.

B. Rule 42.104(b) – Challenge and Relief Requested

Petitioner requests that the Challenged Claims (claims 1-13) of the 288 patent be found unpatentable on the grounds set forth below.

- U.S. Patent No. 5,916,425 ("Leader") was filed on May 16, 1996, issued on June 29 1999, and is prior art at least under 35 U.S.C. § 102(b). Ex. 1003 (Leader) at [22], [45].
- Wang et al., Coated Amperometric Electrode Arrays for Multicomponent Analysis, Anal. Chem. 1990, 62, 1924-27 ("Wang") was published on September 15, 1990 and is prior art under at least 35 U.S.C. § 102(b).

Ex. 1005 (Wang) at 1924-25.

- U.S. Patent Publication No. 2004/0043477 ("Schibli") published in the U.S. on March 4, 2004, and is prior art at least under 35 U.S.C. § 102(b). Ex. 1007 (Schibli) at (43).
- U.S. Patent Publication No. 2004/0189311 ("Glezer") published in the U.S. on Sep. 30, 2004, and is prior art at least under 35 U.S.C. § 102(b). Ex. 1008 (Glezer) at (43).

Ground	Challenged Claims	Statutory Basis for Challenge
1	1, 6-13	Obvious under 35 U.S.C. § 103(a) by Leader in combination with Wang.
2	2-5	Obvious under 35 U.S.C. § 103(a) by Leader in combination with Wang in further view of Schibli.
3	2-5	Obvious under 35 U.S.C. § 103(a) by Leader in combination with Wang in further view of Glezer.

C. Rule 42.104(b)(5) – Evidence Relied Upon

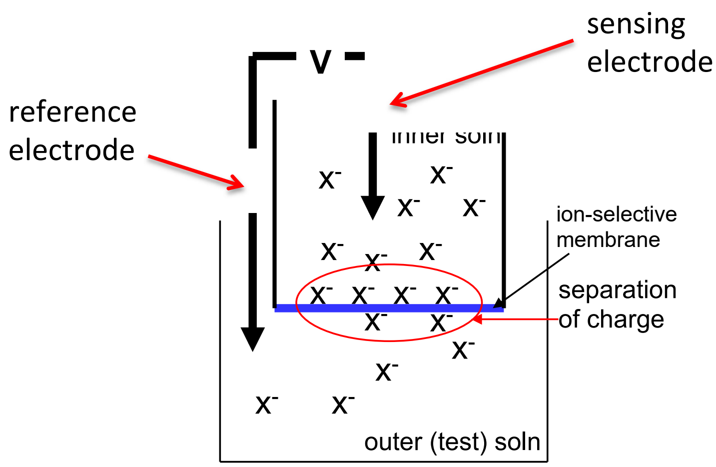
Petitioner relies on the foregoing-listed prior-art references, other exhibits of relevance listed above, and the expert declaration of Dr. Richard M. Crooks (Ex. 1020). In additional to providing Dr. Crook's opinions in detail, Exhibit 1020 includes a claim chart attachment that is a helpful summary of aspects of Dr. Crook's opinions.

Dr. Crooks holds a Ph.D. in electrochemistry from the University of Texas at Austin, and is currently the Robert A. Welch Professor of Materials Chemistry in the Department of Chemistry at The University of Texas at Austin. Ex. 1020 (Crooks Decl.) at ¶¶ 2-3. Dr. Crooks is also the recipient of the Carl Wagner Memorial Award of the Electrochemical Society, a society in which he was awarded lifetime membership. *Id.* at ¶ 4. Dr. Crooks has authored more than 300 peer-reviewed articles, numerous book chapters, and other publications in the field of electrochemistry. *Id.* at ¶ 6. Dr. Crooks's experiences, awards, research, and the like make clear that he is an expert in the field germane to this proceeding.

V. Factual Background

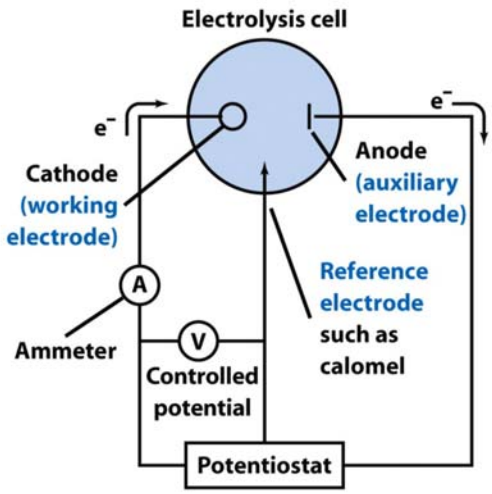
A. Basics of Electrochemical Sensing

In his declaration, Dr. Crooks provides a basic foundation for electrochemical sensing helpful for appreciating the 288 patent and the prior art. *Id.*at ¶¶ 30-32. Potentiometry is the simplest form of electrochemical sensing, and involves measuring the voltage potential at a working or sensing electrode in a sample relative to a reference electrode. *Id.*at ¶ 30. The presence of ions or other analytes within the sample affect the voltage potential and the change in potential may be correlated to analyte concentration. *Id.* Particular analytes may be discriminated from a mixture by coating the working electrode with a membrane selective for a particular analyte. *Id.* In the diagram below, a membrane selective for X renders this cell able to sense the presence of X specifically:



Id. Importantly, no current flows during potentiometric sensing. *Id.*

In contrast, amperometry involves at least two if not three electrodes, where current is passed between a working electrode and an optional counter (or auxiliary) electrode, and the current may then be correlated to analyte concentration. *Id.* at ¶ 31. As shown below, in amperometry, current is flowing between the working and auxiliary electrodes:



Id. In amperometry, unlike potentiometry, because current is flowing, there will be a chemical reaction in the solution as the measurement occurs, changing the composition of the solution and raising the possibility of contaminating the environment of other nearby sensors. *Id.* at ¶ 32

B. Summary of the 288 Patent

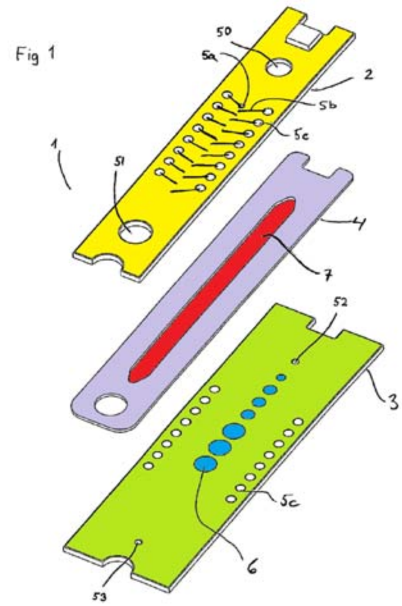
At a high level of generality, the 288 patent describes a "sensor assembly comprising electrochemical sensor elements" that is "suitable for simultaneously measuring a plurality of different parameters, e.g., blood parameters." Ex. 1001 (288 patent) at 1:1-7.[1] Such blood parameters might include partial pressures of blood gases, electrolyte levels, hematocrit, and the like. *Id.* at 1:8-11. More particularly, the 288 patent focuses on devices where the electrochemical sensing occurs in a measuring cell, through which the sample flows past a series of

[1] The citation format XX:YY denotes column:line.

different sensors designed to measure the parameters of interest. *Id.* at 2:38-57.

The 288 patent purports to address a known design imperative particular to the field of blood analysis: minimizing sample size. *Id.* at 1:8-35. Because of high sample frequency ("15-20 per day") or limited blood volume, in the case of neonates, workers in the field sought to minimize sample volumes and maximize the amount of useful information that could be obtained from each sample. *Id.* The desire for small samples led those in the field to focus on building devices with smaller sensors, and with more sensors crowded into smaller flow cells. *Id.* at 1:38-65. "One attempt to solve this problem" that the 288 patent draws from is U.S. Patent No. 5,916,425 ("Leader") (Ex. 1003). *Id.* at 1:37-39. According to the 288 patent, Leader "discloses an electronic wiring substrate for sensors formed over a subminiature through hole" that "allows a relatively large number of sensors to be formed on the surface of the substrate within a relatively small fluid flow cell." *Id.* at 1:40-46. As will be described more fully below, Leader is an example of a typical prior art flow-cell sensor assembly, where the various sensors are disposed along one surface of the flow cell.

The 288 patent purports to improve upon Leader's work addressing the problem of small sample size by describing a "sensor assembly in which several analyte sensors in a very small volume may be positioned in contact with a sample" so that "a smaller sample volume may be used than in similar prior art sensor assemblies without reducing the number of sensors in the sensor assembly." *Id.* at 2:3-15. The 288 patent alleges to have discovered "that it is possible to have fully functional sensor elements placed on opposing walls in a measuring cell," i.e., to place sensors on both sides of a flow cell rather than just one side. *Id.* at 14-16. Thus, the claims of the 288 patent all provide for a measuring cell that has at least two analyte sensors disposed on each of the top and bottom of the cell in a sandwich-like configuration, an example of which is illustrated in Figure 1 of the 288 patent and compared to corresponding claim language (annotated to show the flow cell in red and lower sensors in blue; the upper sensors are obscured from view on the underside of the yellow surface):

288 patent claim 1	288 patent figure 1
1. A sensor assembly comprising: a first electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, a second electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, and a spacer having a through-going recess with a first opening and a second opening, wherein the first substrate, the second substrate and the spacer are arranged in a layered structure, where the first surface of the first substrate closes the first opening of the spacer and the first surface of the second substrate closes the second opening of the spacer, thereby forming a measuring cell in which all the analyte sensors on the first surface of the first substrate face the measuring cell through the first opening of the spacer and wherein all the analyte sensors on the first surface of the second substrate face the measuring cell through the second opening of the spacer, the measuring cell having a shape allowing fluid flow through the measuring cell to be substantially linear.	

However, as demonstrated below, all of the limitations of the claimed invention of the 288 patent were known before April 27, 2007, the earliest priority date arguable for the claims of the 288 patent, and based on the teachings of the prior art, the combinations of those elements in the Challenged Claims would have been obvious. Ex. 1020 (Crooks Decl.) at ¶¶ 47-51 & 71-80.

C. Prosecution History of the 288 Patent

The application for the 288 patent was filed on April 24, 2008, as application no. 12/081,997 (the "997 application"). *See generally* Ex. 1002 (288 patent prosecution history). The 997 application included a claim of priority to EP application 07388028.8, filed April 27, 2007, which Petitioner assumes to be proper for purposes of this IPR.

The original claims of the 997 application are generally similar to the issued claims of the 288 patent — as one example, issued claim 1 of the 288 patent is shown below in comparison with language added by amendment highlighted in yellow.

As filed claim 1	**Issued claim 1**
1. A sensor assembly comprising: a first electronic wiring substrate having a first surface and a second surface and at least one analyte sensor formed on the first surface thereof, the at least one analyte sensor being connected with one or more electrical contact points, a second electronic wiring substrate having a first surface and a second surface and at least one analyte sensor formed on the first surface part thereof, the at least one analyte sensor being connected with one or more electrical contact points, and a spacer having a through-going recess with a first opening and a second opening, wherein the first substrate, the second substrate and the spacer are arranged in a layered structure, where the first surface of the first substrate closes the first opening of the spacer and the first surface of the second substrate closes the second opening of the spacer, thereby forming a measuring cell which is faced by at least one sensor from each of the substrates.	1. A sensor assembly comprising: a first electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, a second electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, and a spacer having a through-going recess with a first opening and a second opening, wherein the first substrate, the second substrate and the spacer are arranged in a layered structure, where the first surface of the first substrate closes the first opening of the spacer and the first surface of the second substrate closes the second opening of the spacer, thereby forming a measuring cell in which all the analyte sensors on the first surface of the first substrate face the measuring cell through the first opening of the spacer and wherein all the analyte sensors on the first surface of the second substrate face the measuring cell through the second opening of the spacer, the measuring cell having a shape allowing fluid flow through the measuring cell to be substantially linear.

Ex. 1002 at April 24, 2008 Claims; Ex. 1001 at claim 1.

On several occasions, the examiner rejected the claims of the 997 application over U.S. Patent No. 6,123,820 ("Bergkuist") (Ex. 1004) in combination with various other references, including Leader. The 288 patent recognizes that Bergkuist also attempted to address the sample size problem by disposing sensors on both sides of a measuring cell, but purports to distinguish Bergkuist based on its "zig-zag flow channel providing a series of sensor ports on both sides of the intermediate part in such a way that each sensor on the two sensor boards is facing a sensor port to form a measuring cell." Ex. 1001 at 1:51-55. The examiner refused to allow the claims over Bergkuist until the applicants made the amendments shown above in yellow. Ex. 1002 at Sept. 19, 2013 Reply & Jan. 9, 2014 Notice of Allowance. The examiner explained that although Bergkuist had "a sensor having two substrates, each having a plurality of sensors disposed thereon, sandwiching a sample cell having openings for the sensors to come into fluidic contact with the sample," Bergkuist lacked "the flow cell having a shape allowing fluid flow through the cell to be substantially linear." *Id.* at Jan. 9, 2014 Notice of Allowance. The examiner considered the possibility that Bergkuist could have been modified to become linear instead of zig-zag, but thought that doing so would have rendered Bergkuist inoperable. *Id.*

Importantly for this IPR petition, the examiner apparently never considered whether a person of ordinary skill in the art, rather than altering Bergkuist's zig-zag design, would have simply started with the one-sided Leader device and made a mirror image, two-sided device. Instead, the examiner considered Leader merely as a possible combination with Bergkuist for certain dependent claims. And the applicants, for their part, recognized that Leader "discloses a single substrate with electrodes," but otherwise did not comment on the reference. E.g., Ex. 1002 at Sept. 15, 2011 Reply, p. 8.

Also importantly for this IPR petition, the examiner did not cite and apparently did not consider Wang (Ex. 1005), Ziegler (Ex. 1006), Schibli (Ex. 1007), or Glezer (Ex. 1008). *See generally id.*

VI. Claim Construction

A. Broadest Reasonable Construction

Pursuant to Office rules, the claim terms of the 288 patent are to be given their broadest reasonable interpretation, as understood by a person of ordinary skill in the art at the time of the invention, consistent with the specification. 37 C.F.R. § 42.100(b). Thus, solely for the purposes of this proceeding and not for any litigation where a different claim-construction standard applies, the following discussion proposes a construction of a phrase used in the claims. Any claim term or phrase not included in the following discussion is to be given its broadest reasonable interpretation in light of the 288 specification as commonly understood by those of ordinary skill in the art

B. "analyte sensor" (claims 1-13)

The term "analyte sensor" would be understood by a person of ordinary skill in the art at the time of the invention to mean "any sensor capable of measuring a physical or chemical parameter, including, but not necessarily limited to, one electrode." *See* Ex. 1020 (Crooks Decl.) at ¶ 39. The evidence for this conclusion is consistent across the claims, specification, file wrapper, prior art, and expert testimony.

"Analyte sensor" appears in both independent claims of the 288 patent, and is referred to as a component of the claimed "sensor assembly" that is formed on the surfaces of the substrates. The claims themselves thus clarify that the "analyte sensor" is a small subcomponent, and not an entire sensing system (for which the phrase "sensor assembly" is being used). The claim language also allows the inference that "analyte sensor" does not include wiring, contacts, substrate, reference electrodes, the analyzer, or the other components claimed elsewhere, not able to be located on "the surfaces of the substrates," or otherwise not part of a "sensor assembly."[2]

Turning to the specification, the 288 patent states expressly that "[i]n this description the term analyte sensor denotes any sensor capable of measuring a physical parameter, such as the concentration of a chemical substance. An analyte

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[2] It is worth clarifying this ambiguity because in common parlance, the term "sensor" might be used to describe an entire sensing system. *See* Ex. 1020 (Crooks Decl.) at ¶ 38. The examiner's Notice of Allowance for the 288 patent is a good illustration of the potential for confusion, using the word "sensor" to mean two different things in a short span of text: "Bergkuist . . . discloses a sensor having two substrates, each having a plurality of sensors disposed thereon." Ex. 1002 at Jan. 9, 2014 Notice of Allowance.

sensor may comprise one o[r] more electrodes and one or more membranes." Ex. 1001 at 7:56-60. Not only is this statement an express definition that governs the interpretation of the term "analyte sensor," but it is also consistent with the remainder of the record evidence. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (en banc) (holding that "the inventor's lexicography governs" where "the specification may reveal a special definition"). In particular, in addition to the definition's allowance that an analyte sensor "may comprise one . . . electrode[]," the remainder of the record evidence is similarly clear that the term analyte sensor can be satisfied by a single working electrode.

Throughout the 288 patent, the term analyte sensor is used to refer to electrodes, including in the primary illustrative embodiment. *See* Ex. 1020 (Crooks Decl) at ¶¶ 40-41. The 288 patent states that each analyte sensor is "connected to an associated electrical contact point," and then implies that such analyte sensors consist of a single electrode by explaining that "in some cases an analyte sensor may be connected to two or more electrical contact points" if, e.g., the analyte sensor comprises "two or more electrodes." Ex. 1001 at 4:33-44. And, by describing the reference electrode as a component separate from the analyte sensor, the 288 patent reinforces that what remains, the working electrode, may be the analyte sensor. *Id.* at 3:27-37.[3]

Consistent with its broad definition for "analyte sensor," the 288 patent does not provide structural details or requirements for its sensors. It does, however, provide a source of example: Leader. The 288 patent describes Leader's sensor arrangement as addressing the same problem as the 288 patent by allowing fabrication in small areas and obtaining "more information" while "using less blood." Ex. 1001 at 1:42-45. The 288 patent also states that examples of the 288 patent's "substrates with analyte sensors maybe found in e.g., [Leader]." *Id.* at 3:1-2. Thus, a person of ordinary skill in the art would understand the use of the phrase "analyte sensor" in the 288 patent in the context of Leader. Leader, in turn, uses the phrase "analyte sensor" to "include at least one electrode" (Ex. 1003 at Claim 21), and provides examples throughout its specification explaining how to fabricate such electrodes (Ex. 1020 (Crooks Decl.) at ¶ 43).

The prosecution file history of the 288 patent is also consistent with this definition. During prosecution, the examiner repeatedly asserted Bergkuist as prior art, and the applicant recognized that in Bergkuist, "[e]ach sensor port is covered

[3] As explained above and detailed by Dr. Crooks (Ex. 1020 (Crooks Decl.) at ¶¶ 30-32), in addition to working electrodes, electrochemical sensors typically include reference electrodes, but the potential of the reference electrode is constant, so any potential difference reflects a change at the working electrode. Hence, and consistent with the descriptions in the 288 patent, Leader, and Bergkuist, while a working electrode falls within the definition of "analyte sensor," a reference electrode typically would not.

by a sensor (32)" and that "each of the claimed substrates carries an analyte sensor." Ex. 1002 at Sept. 15, 2011 Reply, p. 7. Turning to Bergkuist, the reference explains that its sensors 32 had a single "internal sensing electrode 34a." Ex. 1004 at 5:40-50 & Fig. 7. Thus, the applicant's acknowledgment of Bergkuist's applicability to the claim term "analyte sensor" further shows that an "analyte sensor" can be a single electrode.

Finally, the testimony of Dr. Crooks also supports the definition of "analyte sensor" advanced here. Ex. 1020 (Crooks Decl.) at ¶¶ 39-46. Dr. Crooks reached his conclusion upon analysis of the intrinsic evidence as well as a survey of literature uses of the phrase "analyte sensor," which are also consistent with "analyte sensor" corresponding with "electrode," and including a single working electrode. *Id.* at ¶¶ 44-46.

VII. Claims 1-13 of the 288 Patent Are Unpatentable as Obvious Over the Prior Art

A. The Law of Obviousness

The obviousness analysis is objective and determined against the following factual background: "Under § 103, [i] the scope and content of the prior art are to be determined; [ii] differences between the prior art and the claims at issue are to be ascertained; and [iii] the level of ordinary skill in the pertinent art resolved." *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17-18 (1966); *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 407 (2007) ("While the sequence of these questions might be reordered in any particular case, the factors continue to define the inquiry that controls.”). Where available and pertinent, objective considerations of nonobviousness should also be considered, but Petitioner is not aware of any. *Graham*, 383 U.S. at 17-18; *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1349 (Fed. Cir. 2012).

The obviousness analysis is “expansive and flexible,” taking into account “interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art.” *KSR*, 550 U.S. at 415, 417-18 (reversing Federal Circuit finding of nonobviousness for a claim directed to a position-adjustable pedal assembly with an electronic pedal position sensor attached to a fixed pivot point because all of the claimed elements were known and it was obvious to try a combination of these known elements to develop the claimed invention). In that regard, “when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious.” *Id.* at 417 (internal quotations omitted). Further, “if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person’s skill.” *Id.*

at 401; *see also ACCO Brands Corp. v. Fellowes, Inc.*, 813 F.3d 1361, 1366 (Fed. Cir. 2016) (observing that the prior art was well-known and could be combined with predictable effect, and finding obviousness as a matter of law); *Q. I. Press Controls, B.V. v. Lee*, 752 F.3d 1371, 1379-80 (Fed. Cir. 2014) (noting that combination would yield predictable results). Lastly, the analysis also recognizes that "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton" and thus can be expected to "pursue the known options within his or her technical grasp." *KSR*, 550 U.S. at 421.

B. Level of Ordinary Skill in the Art

Dr. Crooks considered the various factors involved in determining the level of ordinary skill (*see Daiicchi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254, 1256 (Fed. Cir. 2007)), and concluded that, generally speaking, the relevant art area is chemical sensing, and in particular, electrochemical sensing of analytes. Ex. 1020 (Crooks Decl.) at ¶ 22. Dr. Crooks explained that the relevant art also includes details of flow and flow-cell design, aspects of which are part of the field of chemical sensing, which embraces flow-based sensing devices. *Id.* at ¶ 23.

In his opinion, an artisan of ordinary skill in this area at the time of the invention would have had a doctoral degree in analytical chemistry, electrochemistry, or electrochemical engineering, or alternatively, an advanced course in electrochemistry or instrumental analysis and a B.S. or M.S. degree in a science or engineering field along with appropriate experience. *Id.* at ¶ 27.

As Dr. Crooks further explains, by 2007, the field of electrochemistry was "highly evolved," and the concepts of potentiometry and amperometry were well known for the measurement of ions, gases, and biomolecules present in test solutions, as were related concepts of flow in channels. *Id.* at ¶ 24-26.

C. Overview of the Prior Art

As outlined above, the 288 patent relates to chemical sensing, and purports to address a problem arising in context of flow-cell based devices for analyzing blood. Hence, this IPR petition identifies and relies on close prior art also in the field of flow-cell based analyte sensing, proves that the 288 patent's alleged problem and solution were both known, and shows that it would have been obvious to a person of ordinary skill in the art to combine it in the same way as the 288 patent claims. The primary reference, Leader, was identified in the specification of the 288 patent and applied for certain purposes by the examiner during prosecution, but at no point did the applicants or examiner appear to consider the obviousness of a two-sided version of Leader, nor did the applicants or examiner appear to have the other key references available to them: Wang, Ziegler, Schibli, or Glezer.

1. Scope and Content of U.S. Patent No. 5,916,425 ("Leader") (Ex. 1003)

Leader, entitled "Electronic Wiring Substrate with Subminiature Thru-

Holes," was filed on May 16, 1996. Ex. 1003 (Leader) at [22], [54]. Leader, therefore, is prior art under at least 35 U.S.C. § 102(b). Like the 288 patent, Leader was directed to the field of flow-cell based devices for electrochemical sensing of blood analytes. *Id.* at 1:5-45; Ex. 1020 (Crooks Decl.) at ¶ 52. Specifically, as shown in Figures 12 & 13, Leader disclosed cartridges with linear flow cells, along which electrochemical sensors were disposed for measuring analytes:

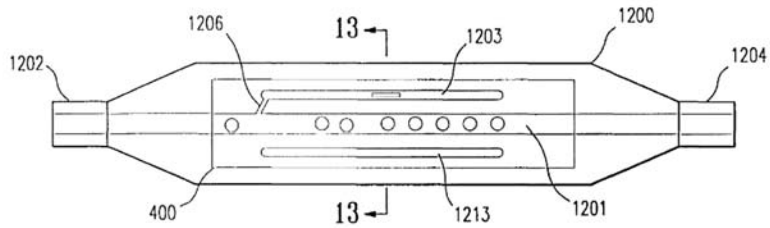


FIG. 12

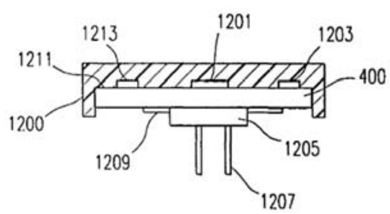
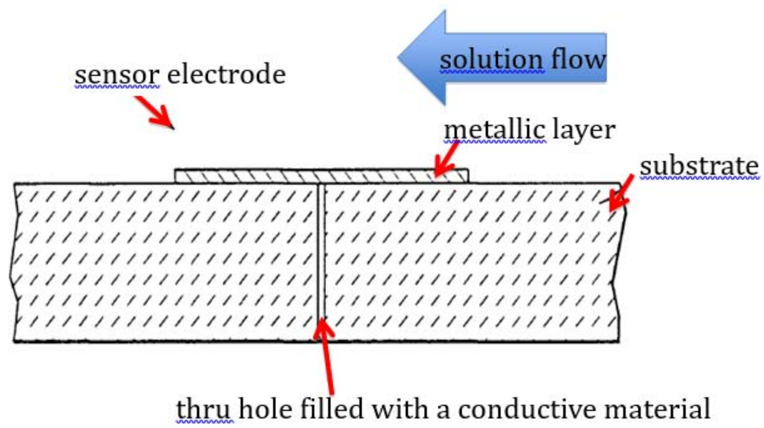


FIG. 13

In the above figures, the Leader sensor assembly 400 and an encasement 1200 enclosing it is shown in a top view (Figure 12) and in cross-section (Figure 13). Ex. 1003 at 20:5-10. The analyte sensors are shown as 403 in other figures (e.g., Figure 2), and correspond to the small circles within the flow cell 1201 in Figure 12, and were disposed along the bottom of the flow channel from the perspective of Figure 13. *Id.* at 20:63-65.

As explained in the 288 patent, the innovation of Leader involved "an electronic wiring substrate for sensors formed over a subminiature through hole." Ex. 1001 at 1:37-39. Figure 9 of Leader showed the structure of these sensors and through-holes, which Dr. Crooks annotated as shown:



Ex. 1020 (Crooks Decl.) at ¶ 53. As Dr. Crooks explained, Leader's structure prevents contact between the flowing solution and the sensor circuitry, and allows for significant miniaturization of the device. *Id.* at ¶¶ 53-54. Leader touted the advantages of its design as follows: "Accordingly, a relatively large number of sensors can be formed on the surface of the substrate within a relatively small sample path. Thus, more information can be attained using less blood." Ex. 1003 at 4:7-13; *see also* Ex. 1001 (288 patent) at 1:39-43; Ex. 1020 (Crooks Decl.) at ¶ 54.

2. Scope and Content of Joseph Wang et al., *Coated Amperometric Electrode Arrays for Multicomponent Analysis*, 62 Anal. Chem. 1924-27 (1990) ("Wang") (Ex. 1005)

Wang is a 1990 publication in the journal Analytical Chemistry entitled "Coated Amperometric Electrode Arrays for Multicomponent Analysis." Ex. 1005 at 1924. Wang, therefore, is prior art under at least 35 U.S.C. § 102(b). Wang was addressing the problem of using "chemically modified electrodes as chemical sensors," for various applications including "flow-injection detection of neurochemically important compounds." *Id.* at 1924. To perform his experiments, Wang described the construction of a "four-electrode thin-layer flow cell" shown in Figure 1 and reproduced below:

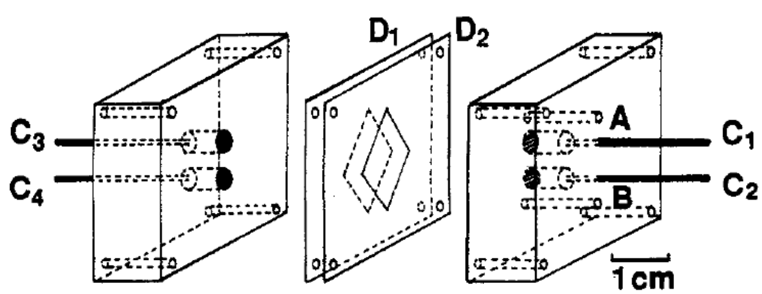


Figure 1. Expanded view of the thin-layer flow cell: (A, B) solution inlet and outlet; (C_1–C_4) working electrodes; (D_1, D_2) spacers.

Id. at 1924-25. Wang described his flow cell as consisting of "two dual electrode (glassy carbon) half cells (Model MF 1000, Bioanalytical Systems (BAS)," and reported that "[o]ne of the blocks was drilled to accept the solution inlet and outlet tubings." *Id.* at 1924. In order to create space for flow from inlet A to outlet B, "[t]he two blocks were separated by two Teflon gaskets (TG-15M, BAS)," shown as D_1 and D_2 in the above figure. *Id.*

By combining these commercially available components in this way, Wang was able to create a flow cell containing two electrodes on each of a top and bottom substrate, facing each other through the cell. Wang coated each of his four electrodes with a different partially selective material, and then used a pattern recognition approach to identify mixture components. *Id.* at 1926. As Dr. Crooks explained, the purpose of this approach was "to extract as much chemical information from as little sample solution as possible," and this could have been equally done with a potentiometric approach as an amperometric approach, without changing the design of Wang. Ex. 1020 (Crooks Decl.) at ¶ 56.

3. Scope and Content of U.S. Patent Publication No. 2004/0043477 (published Mar. 4, 2004) ("Schibli") (Ex. 1007)

Schibli, entitled "Biosensor and Method of Production Thereof," is a U.S. patent application that published on March 4, 2004. Ex. 1007 (Schibli) at (43). Schibli, therefore, is prior art under at least 35 U.S.C. § 102(b). Schibli generally described a three-layer biosensor, one of example of which is shown below:

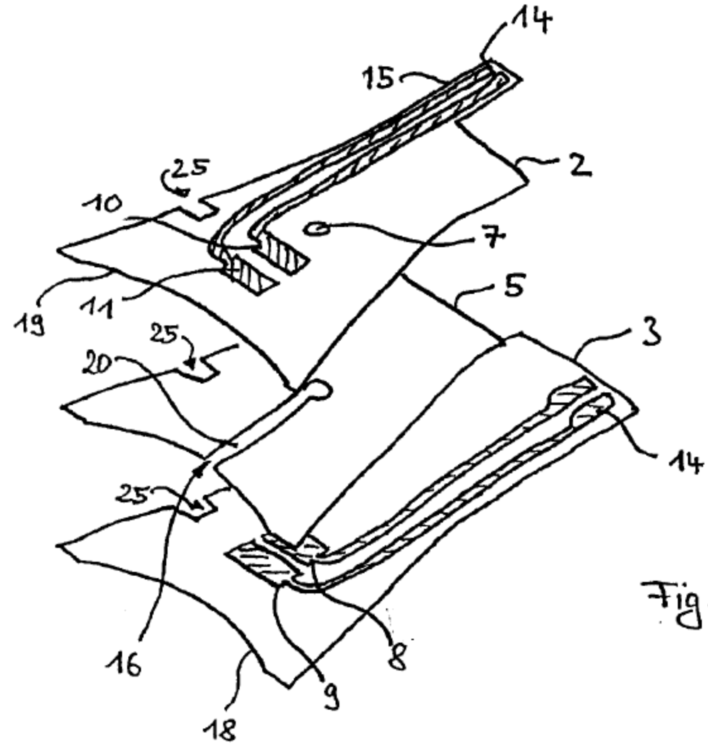


Fig. 1

In Schibli, blood or other body liquid is drawn into a capillary channel 20, where it comes into contact with two electrodes on the top surface and two on the bottom surface (8-11). Ex. 1007 at [0039]-[0041]; *see also* Ex. 1020 (Crooks Decl.) at ¶ 67 (explaining that Schibli described its configuration expansively). Of particular relevance here, Schibli included contacts 14 connected to its electrodes, and Schibli shows those contacts all facing upward in Figure 1. Ex. 1020 (Crooks Decl.) at ¶ 66.

4. Scope and Content of U.S. Patent Publication No. 2004/0189311 (published Sep. 30, 2004) ("Glezer") (Ex. 1008)

Glezer, entitled "Assay Cartridges and Methods of Using the Same," is a U.S. patent application that published on September 30, 2004. Ex. 1008 (Glezer) at (43). Glezer, therefore, is prior art under at least 35 U.S.C. § 102(b). Glezer disclosed designs for assay cartridges for use in biochemical assays. Glezer follows a multi-layer design approach similar to other prior art discussed in this petition, and shown in Figures 13(a) and 13(b):

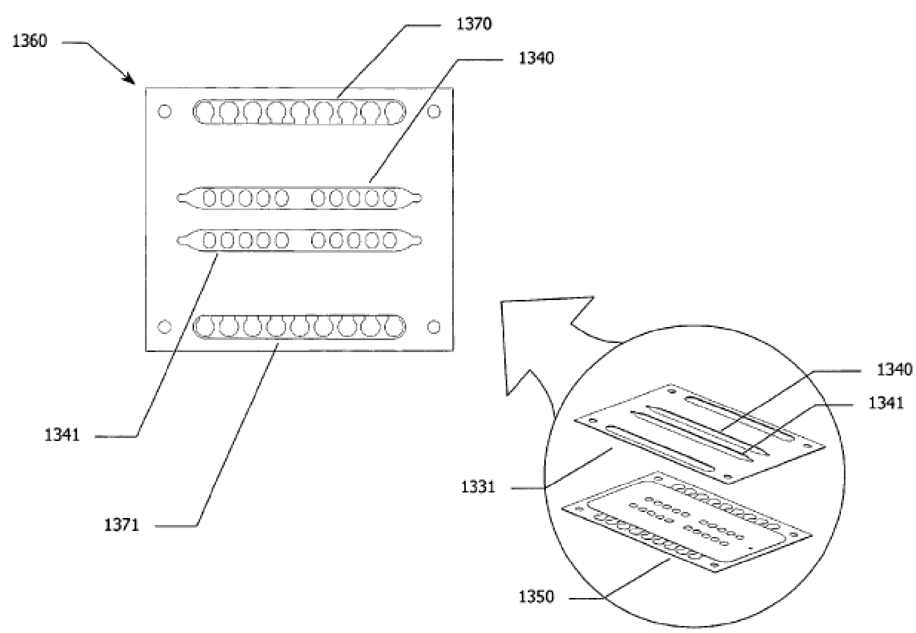


Fig. 13b

Figure 13(b) shows sensors visible through cutouts in a gasket layer that form a path for fluid flow over the sensors. Ex. 1008 at [0220], [0232]-[0233]. Thus, generally speaking, Glezer, like Leader, depicts a single-sided flow cell sensor assembly. In Glezer, the contacts face the same direction as the sensors (shown visible through cutouts 1371, but Glezer teaches that the sensors could be wired to face either direction as convenient. *Id.* at [0234] & [0102]; *see also* Ex. 1020 (Crooks Decl.) at ¶¶ 68-70.

5. Scope and Content of U.S. Patent No. 6,652,810 ("Ziegler") (Ex. 1006)

Ziegler, entitled "Measuring Chamber with Luminescence-Optical Sensor Elements," was filed on November 28, 2000. Ex. 1006 (Ziegler) at [22], [54]. Ziegler, therefore, is prior art under at least 35 U.S.C. § 102(b). Ziegler is yet another flow-through sensing device in the field of blood analysis. Ex. 1006 at 1:15-25. Ziegler's flow channel is lined with optical sensors 4 rather than electrochemical sensors, as shown in Figure 11:

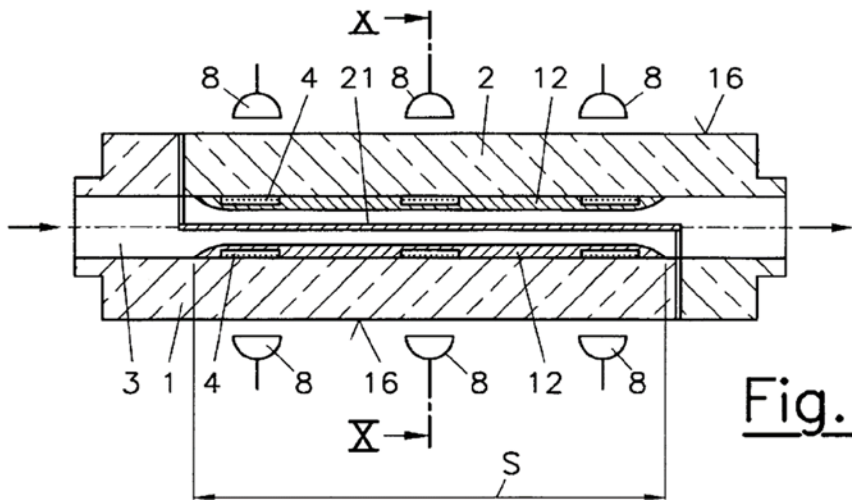


Fig.11

Although Ziegler focused on its optical sensing embodiment, it also taught that its design could be adapted for various uses, including sensor elements for a variety of blood gases and electrolytes. *Id.* at 2:53-3:8; *see also* Ex. 1020 (Crooks Decl.) at ¶ 79. Furthermore, the 288 patent notes that optical sensors are one type of "analyte sensor." Ex. 1001 at 3:27-30 ("the analyte sensors . . . are preferably . . . an optical sensor . . . .").

D. The Prior Art Identified the Goal of Reducing Sample Size and the Solution of Disposing Sensors on Both Sides of the Flow Cell

As discussed above, the 288 patent purports to address the problem of how to minimize sample size in the field of blood analysis. But the inventors of the 288 patent did not recognize this problem first, nor did they address it in a new way. Rather, sample-size reduction was a shared goal in the field before 2007, and the 288 patent's purported solution was already known.

The prior art of record in this IPR petition demonstrates the shared desire in the field to reduce sample size. Leader establishes this goal as follows:

> In addition, in an attempt to use as little of the patient's blood as possible in each analysis performed, the devices which are employed to analyze a blood sample are preferably relatively small. Performing blood analysis using a small blood sample is important when a relatively large number of samples must be taken in a relatively short amount of time or if the volume of blood is limited, as in neonates. For example, patients in intensive care require a sampling frequency of 15-20 per day for blood gas and clinical chemistry measurements, leading to a potentially large loss of blood during patient assessment. In addition, by reducing the size of the analyzer sufficiently to make the unit portable, analysis can be performed at the point of care. Also, reduced size typically means reduced turnaround time. Furthermore, in order to limit the number of tests which must be performed it is desirable to gather as much information as possible upon completion of each test.

Ex. 1003 (Leader) at 1:20-38. The alignment of problems addressed between Leader and the 288 patent is particularly clear because much of the same language is used to set forth the problem in the two documents. *Compare* Ex. 1003 (Leader) at 1:20-38 *with* Ex. 1001 (288 patent) at 1:19-28.[4]

Leader's miniaturization techniques, discussed above, helped address the sample size problem by allowing more sensors to be fabricated in a smaller area. And the 288 patent recognized that Leader achieved this goal, and thus incorporated Leader's sensors and wiring substrates. Ex. 1001 (288 patent) at 1:42-46 & 2:65-3:2. But others in the field also recognized the need to improve. Bergkuist also focused its efforts on assessing the multiple chemical constituents of "small volume samples of bodily fluids (e.g., whole blood)" and stated that miniaturized planar sensors configured closely together can "reduc[e] the sample volume requirements." Ex. 1004 (Bergkquist) at 1:8-10 & 1:46-50; *see also id.* at 1:67-2:6 (explaining ways to limit sample volume requirements). Ziegler, Schibli, and Glezer also recognized the volume problem. Ex. 1006 (Ziegler) at 2:14-16; Ex. 1007 (Schibli) at [0007]; Ex. 1008 (Glezer) at [0216]. And as Dr. Crooks explained, miniaturization has long been a goal in the field. Ex. 1020 (Crooks Decl.) at ¶¶ 49-50 (citing Meyerhoff (Ex. 1010)).

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[4] Presumably, the reason that the 288 patent and Leader share language and common technology is that the 288 patent represents further work from the same company that patented Leader. The owner of the 288 patent, Radiometer, purchased the assignee named on the face of Leader, Sendx Medical, Inc. not long after Leader was filed. According to USPTO records, Leader was assigned to Radiometer in 1998.

There is more than one way to reduce the sample volume in flow cell sensor assemblies — or more generally, increase the sensor density on a per volume basis. Some of these ways are addressed by the prior art discussed above: miniaturize the sensors (Leader) or position the sensors outside the flow channel so that the width of the channel may be reduced to less than the width of the sensors (Bergkuist, e.g., Ex. 1004 at 8:50-67). *See also* Ex. 1020 (Crooks Decl.) at ¶ 50. Dr. Crooks laid out three ways to increase sensor density, all of which he concludes would have been obvious: "(1) reduce the size of the individual sensors and move them closer together; (2) reduce the dimensions of the flow cell to minimize the interior volume; (3) insert additional sensors into a particular, fixed volume." Ex. 1020 (Crooks Decl.) at ¶ 50. Leader corresponds to the first way, and Bergkuist to the second way. The third way, which was adopted by the 288 patent by virtue of its disposing sensors on the top and bottom of the flow cell, was expressly taught by Wang (described in much more detail below), Schibli (also discussed below) and Ziegler.

Ziegler expressed the object of "permitting a greater number of individual parameters to be determined while using essentially the same sample volume as before." Ex. 1006 (Ziegler) at 2:14-16. Axiomatically, this goal of increasing sensor density would equally achieve decreased sample volume for the same number of parameters to be determined. Ziegler taught (and demonstrated) that the way to achieve this goal was to dispose sensors along both the top and bottom of the flow channel instead of just the top or bottom:

> According to the invention this object is achieved by providing a longitudinal groove each in the bottom part and in the top part, which grooves together form the measuring channel, and by arranging for sensor elements to be placed in the longitudinal grooves of the bottom part and the top part, each of which elements is coated with an optical cover layer covering the entire sensing area. These provisions of the invention will allow the number of luminescence-optical sensor elements to be doubled while the sample volume will essentially remain the same, as the sensor elements will be positioned in the bottom part as well as in the top part.

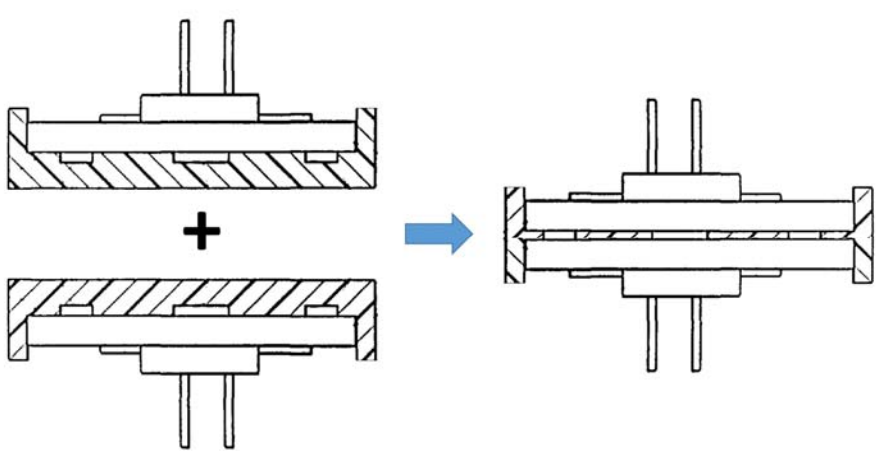
Ex. 1006 at 2:17-27. Ziegler further taught that this dual-sided configuration could be implemented symmetrically, with the surfaces facing each other (*id.* at 2:54-56), and that the sensors could be placed in opposing pairs (*id.* at 4:9-11). Thus, a person of ordinary skill in the art would have been well aware of the problem addressed by the 288 patent, and would have been in possession of the exact solution to the sample-size problem that the 288 patent adopted. Ex. 1020 (Crooks Decl.) at ¶¶ 50, 55, 79. As discussed in detail below, that solution is embodied by Wang, and it would have been obvious to combine Leader and Wang to obtain the benefits of that solution.

E. A Person of Ordinary Skill in the Art Would Have Followed Wang to Create a Two-Sided Version of Leader ("Leader-Wang")

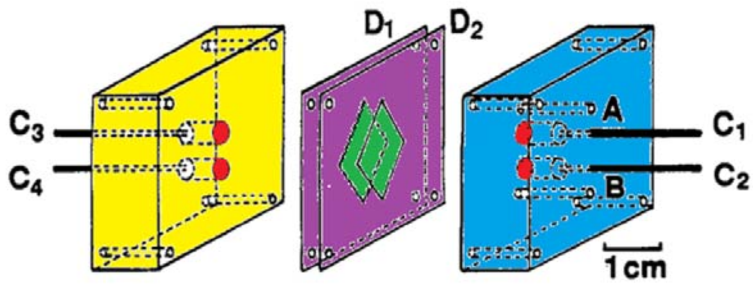
As explained above in section VII(D), a person of ordinary skill in the art, working with the Leader reference, would have been motivated to increase the sensor density of Leader in order to reduce blood sample volume. Having already obtained the fabrication advantages of the Leader design discussed above, a person of ordinary skill in the art would have been led to consider a design similar to Leader, but with sensors on both surfaces of the flow cell rather than just a single surface. As discussed above, the skilled artisan would have pursued the two-sided design as a solution to the sample volume problem because (i) this was one of the few ways available to increase sensor density and (ii) Wang and Ziegler expressly taught this solution. Ex. 1020 (Crooks Decl.) at ¶¶ 50 & 79; Ex. 1006 (Ziegler) at 2:17-27.

A person of ordinary skill in the art, starting with Leader and seeking to modify its design to provide for sensors on both sides of the flow channel, would have confronted the problem of what to put between the two sensor-bearing substrates to form a flow cell. In Leader, the plastic cover 1200 sits atop the sensor assembly 400 and creates the flow cell. Ex. 1020 (Crooks Decl.) at ¶¶ 75-76. With two sensor assemblies instead of a cover, the ordinarily skilled artisan would have had to provide a flow cell between the sensor assemblies. *Id.* The simplest solution to this design problem is provided by Wang, and a person of ordinary skill in the art would have found it obvious to adopt the design of Wang's flow cell to create a two-sided version of Leader. *Id.* Wang would have been a particularly attractive and inspirational approach to modifying Leader, because Wang's design process paralleled that of the skilled artisan modifying Leader. Namely, in Wang, the authors started with an existing, one-sided planar substrate with two analyte sensors, mirrored it with another identical planar substrate with two sensors, and used an intermediate layer to create space for the fluid to flow. Ex. 1005 (Wang) at 1924. So too, starting with Leader, a person of ordinary skill in the art would have taken the one-sided planar substrate with analyte sensors, mirrored it with another identical planar substrate with analyte sensors, and used an intermediate layer to create space for the fluid to flow. Ex. 1020 (Crooks Decl.) at ¶¶ 76-77. Dr. Crooks explained that the close structural compatibility of Leader and Wang would have made it simple for a person of ordinary skill in the art to follow this design process. *Id.*

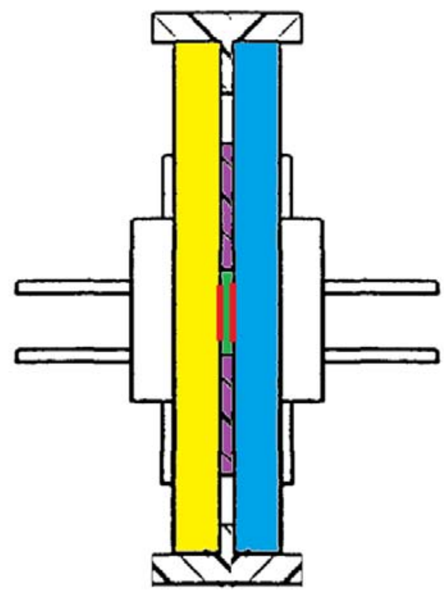
The process where a person of ordinary skill in the art would have used the Wang design to modify Leader can be depicted visually by modifying the cross-sectional Figure 13 in Leader as follows:



Id. at ¶ 76. The close structural analogy between this modified Leader and Wang is shown below (note that Wang is shown in a side-3D view, with the line of sensors going vertically, and modified Leader is shown in a cross-section, with the line of sensors going into and out of the page):



Wang



Leader (modified)

Id. at ¶ 77. In this diagram, above, the two substrates are shown in blue and yellow; the intermediate layer is shown in purple; the flow cell is shown in green; and the sensors are shown in red. As can be readily seen, Wang's method for making a two-sided sensor assembly out of two single-sided sensor assemblies would have been obviously applicable to Leader. *Id.* As will be explained below, the resulting modified Leader meets all the limitations of most of the Challenged Claims, and for that matter, is essentially identical to the 288 patent's preferred embodiment.

F. There Would Have Been Nothing Surprising About the Combination of Leader and Wang

Neither Leader, nor Wang, nor the other prior art of record indicates any reason why a person of ordinary skill in the art would have been dissuaded from combining Leader and Wang. Indeed, in that combination, each component of Leader and Wang is performing exactly the function that it performed separately, and what results is exactly what would have been expected, which is a powerful indicator of obviousness. *KSR*, 550 U.S. at 417; *ACCO Brands*, 813 F.3d at 1366; *Q. I. Press Controls,* 752 F.3d at 1379-80. Although the 288 patent appears to suggest the presence of unexpected results in the form of overcoming "interference," these statements do withstand scrutiny and may be disregarded.

In spite of the lack of evidence in the prior art, and without citation, the 288 patent alleges that the functionality of a two-sided sensor assembly is somehow surprising or unexpected. *See* Ex. 1001 (288 patent) at 2:14-16 ("[I]t has surprisingly appeared that it is possible to have fully functional sensor elements placed on opposing walls in a measuring cell"); *id.* at 2:43-46 ("It has unexpected[ly] appeared that it is possible to measure two or more parameters in the same measuring cell, without any significant interference between opposing analyte sensors, although no walls, channels, or the like are present to keep the analyte sensors separated."). These statements in the 288 patent should be disregarded, because they lack any factual basis. *In re De Blauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual evidence. Mere argument or conclusory statements in the specification does not suffice."); *see also In re Wood*, 582 F.2d 638, 642 (CCPA 1978) ("Mere . . . conclusory statements in the specification, unsupported by objective evidence, are insufficient to establish unexpected results."); *In re Lindner*, 457 F.2d 506, 508 (CCPA 1972) ("[M]ere conclusory statements in the specification . . . are entitled to little weight when the Patent Office questions the efficacy of those statements.").

Contrary to the conclusory statements in the 288 patent specification, the combination of Leader and Wang would not have had any surprising functionality, and would not have been susceptible to any special interference problems because of its dual-sided nature.

Dr. Crooks explains in his declaration that the concept of "interference" in electrochemical sensing is associated with amperometric sensing rather than potentiometric sensing, because potentiometric sensing does not change the composition of the solution in the flow cell, whereas amperometric sensing does. Ex. 1020 (Crooks Decl.) at ¶¶ 32-33. Thus, depending upon the placement of the amperometric sensors relative to other sensors, and the fluid flow parameters, the operation of an amperometric sensor could significantly influence what other sensors detect. *Id.* at ¶¶ 33.

The possibility of interference, however, plays no role in this IPR petition for several reasons. First, the claims of the 288 patent do not require any particular type of analyte sensor or operating in potentiometric or amperometric mode. Therefore, a person of ordinary skill in the art could have implemented the Leader-Wang combination with all potentiometric sensors, or at least used only potentiometric sensors where sensors are placed in close proximity, and/or place amperometric sensors downstream, and avoided interference problems. *Id.* at ¶ 35-36. Indeed, Dr. Crooks's view is that this is a possible explanation for the 288 patent's statement that no interference was observed. *Id.* at ¶ 34.

Second, the claims of the 288 patent do not require any particular spacing of the analyte sensors. Therefore, a person of ordinary skill in the art could have simply selected spacing and fluid flow parameters to avoid significant interference. *Id.* at ¶ 33. Indeed, rather than specify spacing of the sensors, the 288 patent states only that "[i]t is preferred that the spacing between the individual analyte sensors on the same substrate and the spacing between analyte sensor on the first substrate and an analyte sensor on the second substrate should have an extension sufficient to avoid interference between the different sensors." Ex. 1001 (288 patent) 4:1-5. This alleged "preference" is not captured in any claims of the 288 patent.

Third, a person of ordinary skill in the art working with Leader and Wang would have had particularly little concern about interference, because neither of those references reported any significant interference problems. From Leader, a person of ordinary skill in the art would have understood that miniaturized sensors can be used in tight proximity without interference problems, and would not have seen any reason why tight proximity across the channel would be any different than tight proximity along the channel. Ex. 1020 (Crooks Decl.) at ¶ 57. From Wang, a person of ordinary skill in the art would have appreciated that electrodes can be closely spaced across a flow cell and still act independently with no barrier. *Id.*

In view of all the evidence, Dr. Crooks concluded that the statements about interference and unexpected results in the 288 patent are simply false, because the claims of the 288 patent impose no design constraints that necessitate confronting interference problems, and because the prior art relied upon raises no concerns. *Id.*

G. Independent Claim 1 Would Have Been Obvious Over Leader-Wang

The discussion above is the foundation for the obviousness analysis below. A person of ordinary skill in the art would have found it obvious to combine Leader and Wang to form a two-sided version of Leader ("Leader-Wang"). A person of ordinary skill in the art would have pursued Leader-Wang in order to advance the universal goal of reducing sample size in flow-cell based blood analyzers, recognized in Leader, and would have used the two-sided solution that is both so basic that it would have been readily apparent, and moreover was taught expressly by Wang and Ziegler. For reference in the obviousness analysis, below is a colored and labeled version of Leader-Wang:

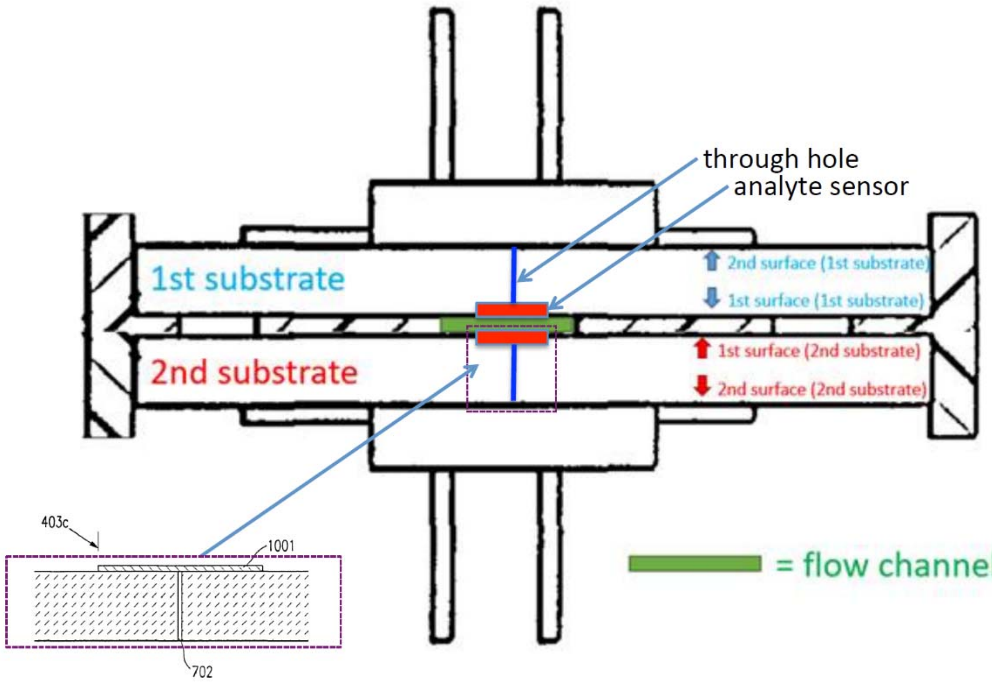


Fig. 9 from Leader

As explained by Dr. Crooks, this figure shows two Leader sensor assemblies in a sandwich, with a Wang-type spacer in between to create a flow cell, shown in green. Ex. 1020 (Crooks Decl.) at ¶ 76. As pointed out by Dr. Crooks, a person of ordinary skill in the art would have simply adapted the spacer to fit the shape of Leader. *Id.* In Leader, the sensors are not shown in Figure 13, so Dr. Crooks illustrated them in red, and provided Figure 9 in an inset to illustrate the pad and through-hole wiring. *Id.* It should be noted that with respect to most of the claims, the denotation of first and second substrate is interchangeable.

1. Preamble: "A sensor assembly"

To the extent that the preamble here is limiting, both Leader and Wang taught sensor assemblies. Leader's sensor assembly is typically denoted 400. *See, e.g.*, Ex. 1003 (Leader) at Figures 2 & 12; *id.* at 5:22-23 & 5:53-54; Ex. 1020 (Crooks Decl.) at ¶ 82. Wang also taught a sensor assembly, shown in Figure 1 and described as a "thin-layer flow cell." Ex. 1005 (Wang) at Figure 1; Ex. 1020 (Crooks Decl.) at ¶ 83. The Leader-Wang combination therefore also includes a sensor assembly.

2. Limitation 1: "a first electronic wiring substrate"

Leader-Wang taught "a first electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points." There can be little doubt that Leader teaches the 288 patent's claimed electronic wiring substrates and analyte sensors, because the 288 patent states that Leader "discloses an electronic wiring substrate for sensors formed over a subminiature through hole." Ex. 1001 (288 patent) 1:36-42. The 288 patent also states that "[e]xamples of such substrates with analyte sensors may be found in" Leader. *Id.* at 3:1-2; *see also* Ex. 1020 (Crooks Decl.) at ¶ 85.

In Leader, there is one electronic wiring substrate, typically labeled 405, but also as 30 in Figure 1 with respect to prior art. Thus, in Leader's terms, the "first surface" of the first electronic wiring substrate is the top surface of 405, i.e., the surface that faces the flow cell and has sensors disposed on it. In Figure 2, for example, the first surface is shown and the second surface is hidden from view; in Figures 8 and 9, the first surface is toward the top and the second surface is toward the bottom; in Figure 13, the substrate is the bulk of the sensor assembly 400, with the first surface facing up and second surface facing down. Ex. 1020 (Crooks Decl.) at ¶ 86.

Leader also taught at least two sensors formed on its first surface, for example shown in top view in Figure 12. Ex. 1020 (Crooks Decl.) at ¶ 87. Claim 1 of Leader also recites "a plurality of analyte sensors deposited on the first side planar surface of the substrate." Ex. 1003 (Leader) at 22:16-22. Furthermore, Leader's analyte sensors are connected with electrical contact points as shown in Figure 9, where the conductive filling in the through hole (702) connects to the back of the metallic layer (1001) at the contact. Ex. 1020 (Crooks Decl.) at ¶ 88. In Figure 13, this assembly then connects to an external connector structure (1205, 1207, 1209).

Wang also includes a first electronic wiring substrate (the left side of the thin-layer flow cell shown in Figure 1 of Wang) that has disposed on it two analyte sensors, shown as "working electrodes" C_3 and C_4. Ex. 1005 (Wang) at 1924-25; Ex. 1020 (Crooks Decl.) at ¶¶ 88-89. The working electrodes are connected to an analyzer via contact points. Ex. 1005 (Wang) at 1924; Ex. 1020 (Crooks Decl.) at ¶ 90.

3. Limitation 2: "a second electronic wiring substrate"

Leader-Wang taught "a second electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points." As explained above, and incorporated here, a person of ordinary skill in the art would have been motivated to create a two-sided version of Leader using two copies of Leader's "first electronic wiring substrate" (described above and shown in the Leader-Wang figure below):

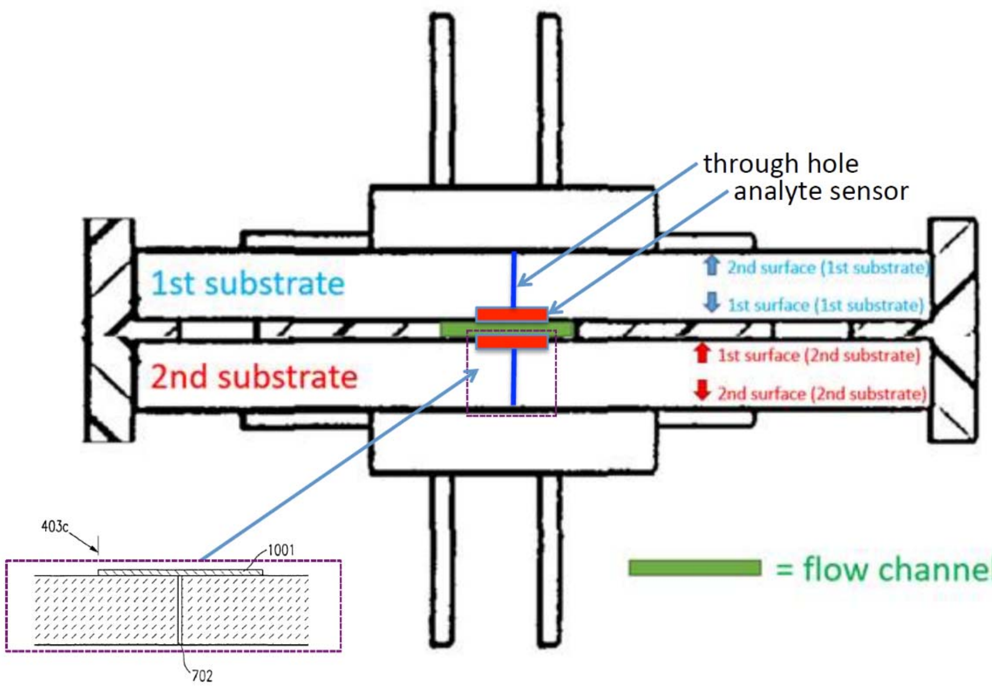
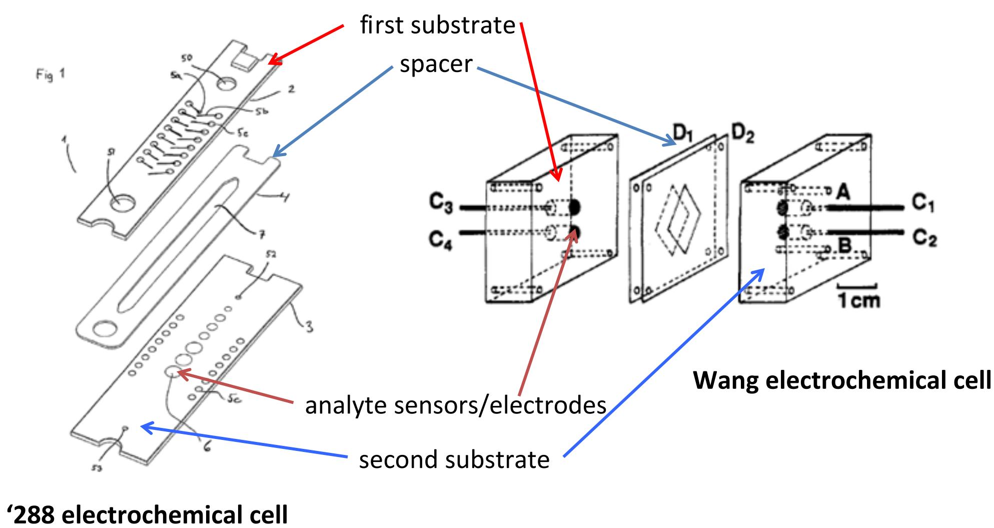


Fig. 9 from Leader

Ex. 1020 (Crooks Decl.) at ¶¶ 91 & 93. Thus, all of the teachings of Leader discussed above apply equally to this limitation, with respect to the second substrate that a person of ordinary skill in the art would have added to Leader. *Id.* As shown above, the top substrate is designated the first substrate (with the second surface facing up and first surface facing down) and the bottom substrate is designated the second substrate (with the first surface facing up and the second surface facing down). The analyte sensors are thus disposed on the respective first surfaces of the substrates, facing the flow channel (shown above in green). The through-wiring is to the contact on the back sides of the substrate and is shown in blue.

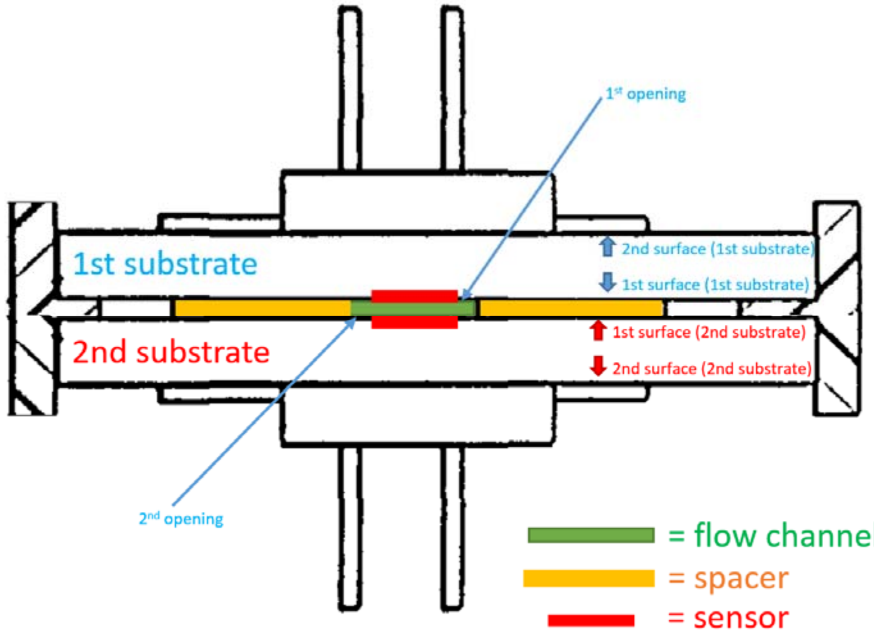
Wang taught both a first and second electronic wiring substrate. In Wang, the second electronic wiring substrate is shown on the right of Figure 1, with two analyte sensors labeled C_1 and C_2, formed on the first surface, and connected with electrical contact points to an analyzer. Ex. 1005 (Wang) at 1924; Ex. 1020 (Crooks Decl.) at ¶ 92. The correspondence of Wang to the 288 patent is shown below:



Ex. 1020 (Crooks Decl.) at ¶ 47. The close analogy between Wang and the 288 patent reinforces the resulting close analogy between Leader-Wang and the 288 patent.

4. Limitation 3: "a spacer having a through-going recess with a first opening and a second opening,"

Leader-Wang taught "a spacer having a through-going recess with a first opening and a second opening." The Wang flow cell includes a through-going recess formed by a spacer consisting of D1 and D2, which are Teflon gaskets, and which define the flow path of the flow cell. Ex. 1005 (Wang) at 1924-25; Ex. 1020 (Crooks Decl.) at ¶ 96. Wang's spacer has a first opening, facing left toward the first substrate, and a second opening, facing right toward the second substrate. Thus, as explained below, when combined with Leader, the resulting Leader-Wang structure will also include a spacer having a through-going recess with a first opening and a second opening, shown below:



Ex. 1020 (Crooks Decl.) at ¶ 97. Leader did not teach a spacer between two substrates, but rather formed its flow cell with a plastic encasement 1200 over the sensor assembly 400. As explained, a person of ordinary skill in the art would have found it obvious to replace the plastic encasement with a second sensor assembly, and make use of a spacer (as taught by Wang) to form the flow cell between the substrates. *Id.* The resulting Leader-Wang structure would thus have a spacer (shown in yellow) that creates a flow channel (shown in green) having first and second openings as indicated. *Id.*

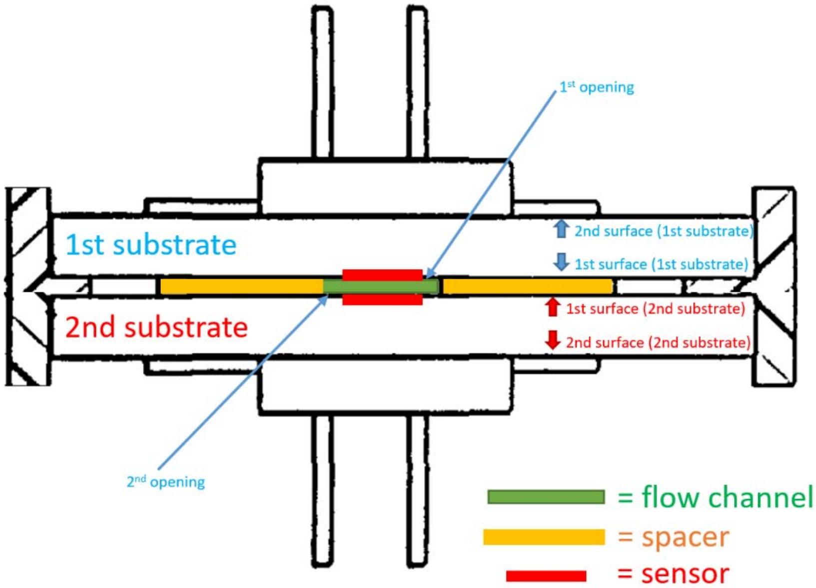
Dr. Crooks explained that although Wang used two gaskets, D_1 and D_2, to form his measuring cell, this was likely because Wang was using commercially available gaskets, and needed to use two to create the flow cell volume he desired. *Id.* A person of ordinary skill in the art would have simply selected a spacer for

Leader-Wang of appropriate shape and size to create the desired flow channel, just as Leader selected a plastic encasement of appropriate size for the same purpose. *Id.* The 288 patent claims, of course, have no dimensional requirements.

5. Limitation 4: "wherein the first substrate … substantially linear"

Leader-Wang taught its configuration "wherein the first substrate, the second substrate and the spacer are arranged in a layered structure, where the first surface of the first substrate closes the first opening of the spacer and the first surface of the second substrate closes the second opening of the spacer, thereby forming a measuring cell in which all the analyte sensors on the first surface of the first substrate face the measuring cell through the first opening of the spacer and wherein all the analyte sensors on the first surface of the second substrate face the measuring cell through the second opening of the spacer, the measuring cell having a shape allowing fluid flow through the measuring cell to be substantially linear."

Leader-Wang's structure possesses the requirements of this limitation, as shown in the diagram below:



First, Leader-Wang shows the first substrate, second substrate, and spacer arranged in a layered structure: the first substrate is the top layer, the second substrate is the bottom layer, and the spacer is in between. Ex. 1020 (Crooks Decl.) at ¶ 99.

Second, in Leader-Wang, the first surface of the first substrate closes the first opening of the spacer and the first surface of the second substrate closes the second opening of the spacer, thereby forming a measuring cell. As shown above, the first opening faces upward toward the first substrate, and the first substrate closes that opening. Likewise, the second opening faces downward toward the second substrate, and the second substrate closes that opening. *Id.* By closing off the two openings of the spacer, the result is the measuring cell shown as a green rectangle (bordered at the top by the first substrate and bordered at the bottom by the second substrate). *Id.*

Third, in Leader-Wang, all the analyte sensors on the first surface of the first substrate face the measuring cell through the first opening of the spacer and all the analyte sensors on the first surface of the second substrate face the measuring cell through the second opening of the spacer. *Id.* at ¶ 100-01. As shown in red in the figure above, the sensors of the first surface of the first substrate are disposed along the top (first) opening of the spacer, facing downward into the measuring cell; and the sensors of the first surface of the second substrate are disposed along the bottom (second) opening of the spacer, facing upward into the measuring cell. *Id.* As with Wang, the spacer in Leader-Wang would have included all the sensors along the surfaces within its openings.

Fourth, in Leader-Wang, the measuring cell has a shape allowing fluid flow through the measuring cell to be substantially linear. As shown in Figure 12, Leader's flow channel is rectangularly shaped, stretching from an inlet to an outlet in a straight line. Thus, Leader-Wang's channel would be similarly straight and rectangular in shape. Therefore, Leader-Wang's shape would allow linear fluid flow. *Id.* at ¶ 102.

Note that Wang alone also taught all aspects of this claim limitation, which further supports the same conclusion for Leader-Wang. *Id.* at ¶¶ 100-103. In

Wang, the two substrates and gasket layer are arranged in a layered structure as shown in Figure 1 of Wang: first substrate – spacer – second substrate, from left to right. Ex. 1005 (Wang) at 1925. In Wang's thin-layer flow cell, the spacer layer has first opening facing left toward the first surface of the first substrate, and a second opening facing right toward the first surface of the second substrate. *Id.* A measuring cell is formed in the diamond-shaped area within the spacer layer when the two openings are closed off by the respective surfaces of the substrates. And, as shown, within that measuring cell, all the analyte sensors on either surface face each other through the openings. Ex. 1020 (Crooks Decl.) at ¶ 100. Finally, the measuring cell allows for linear flow from an inlet to an outlet, which are set linearly apart from one another. *Id.* at ¶¶ 102-03.

H. Dependent Claim 2 Would Have Been Obvious Over Leader-Wang, in Further View of Either Schibli or Glezer

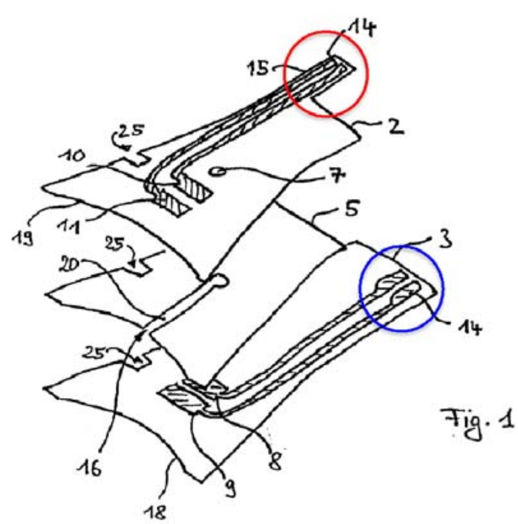
Leader-Wang, in combination with either Schibli or Glezer, renders obvious that "the electrical contact points of the first substrate are arranged on the second surface of the first substrate and wherein the electrical contact points of the second substrate are arranged on the first surface of the second substrate." Because claim 2 depends from claim 1, the analysis of claim 2 incorporates the analysis for claim 1, above, as well as the following.

In the depiction of Leader-Wang shown above, the analyte sensors (disposed on the first surfaces) are wired to contacts on the backs (the second surfaces) of the substrates via through-holes. Claim 2 requires, however, that the contacts all face the same direction. A person of ordinary skill in the art would have appreciated the benefit of this, because Leader and many of the other prior art sensor assemblies are consumable cartridges designed to be plugged into analyzer machines, and therefore, the cartridge-analyzer interface must be reliable and easy to engage. Ex. 1020 (Crooks Decl.) at ¶¶ 106-07.

Because Leader is a one-sided sensor assembly, Leader did not have to be concerned about which direction its contacts faced, because regardless, they would all face the same direction. Ex. 1020 (Crooks Decl.) at ¶ 107. Yet, Leader recognized the importance of the cartridge-analyzer interface, explaining that the contacts of the sensor device are meant to slide against mating contacts in the analyzer, and that robustness of the contacts is important for the design. Ex. 1003 (Leader) at 3:6-16; Ex. 1020 (Crooks Decl.) at ¶ 106. A good design, according to Leader, should afford easy installation and a "reliable interface" to allow for good performance and mass production at low cost. Ex. 1003 (Leader) at 20:21-30; Ex. 1020 (Crooks Decl.) at ¶ 106.

In view of the design need outlined above, it would have been obvious to arrange the contacts in Leader-Wang all facing the same direction, in order to facilitate a simple and reliable cartridge-analyzer interface, and to minimize the changes that would have been needed to existing analyzers when switching from a one-sided design to a two-sided design. A person of ordinary skill would have been further encouraged, and easily able, to rearrange the contacts on one substrate of Leader-Wang using the subminiature-through hole technique of Leader, by simply routing the conductor back through the substrate to the sensor side. Ex. 1020 (Crooks Decl.) at ¶ 107.

The obviousness of claim 2 is further reinforced by either of two additional prior art references in the field: Schibli and Glezer. Schibli's electrodes are wired to contacts 14, and as shown, the upper contacts (red circle) face upward, and the lower contacts (blue circle) also face upward. Ex. 1007 (Schibli) Figure 1; Ex. 1020 (Crooks Decl.) at ¶ 109. This design facilitates a simple cartridge interface, as it can be seen that Schibli's upper layer is cut out near the numeral 2 to allow the lower contacts to protrude from the upper layer and thus interface with an analyzer.



Ex. 1020 (Crooks Decl.) at ¶ 109. A person of ordinary skill in the art would have adopted this contact design from Schibli and made use of it in Leader-Wang to arrange the Leader-Wang contacts such that they all face the same direction.

Glezer described a one-sided sensor design similar in some ways to Leader, as shown, for example, in Figure 1c:

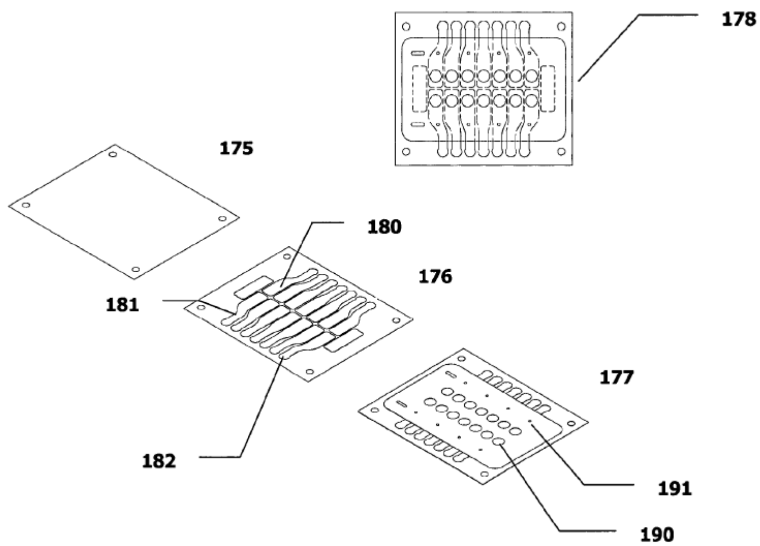


Fig. 1c

Glezer involves linear arrays of electrodes along flow cells, and describes connecting those electrodes to contacts via conductive through-holes, and ultimately, to analyzers via an electro-mechanical cartridge interface. Ex. 1008 (Glezer) at [0253] & Figure 23. Glezer recognizes that design need might call for moving the contacts to either surface of the substrate, and describes how to do that:

> "According to one embodiment, electrode array 176 (preferably, comprised of carbon ink) is applied to the substrate layer 175 forming the electrode 180, electrical lead 181 and electrical contact 182

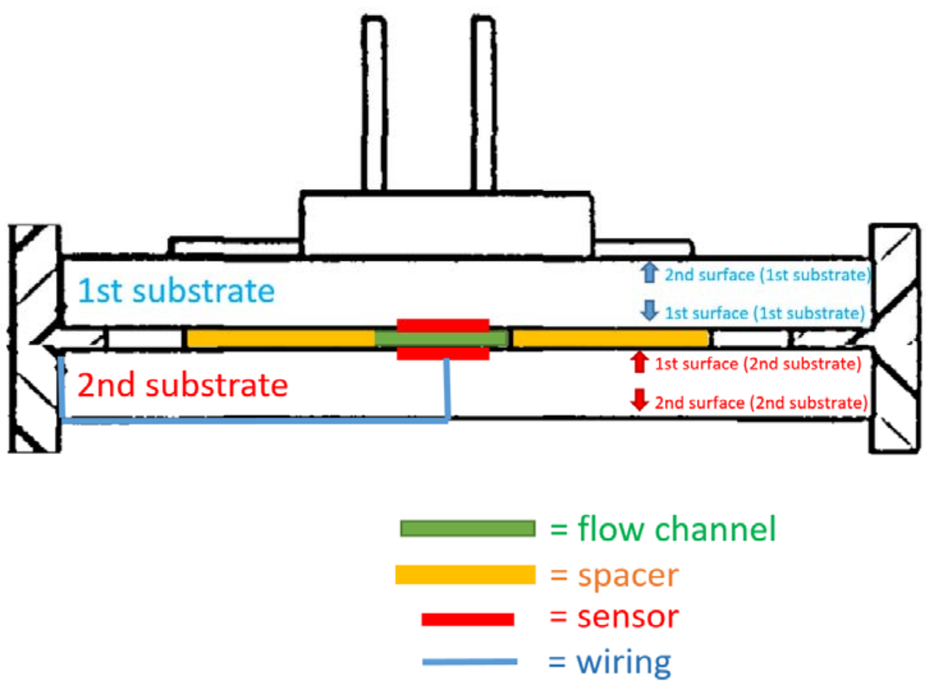
> portions. A dielectric layer 177 is preferably applied over the electrode layer to define the assay domains 190 and the impedance sensors 191. Alternately, electrical contacts 182 could be printed on the opposing side of the substrate and connected to electrodes 180 or electrical leads 181 via conductive through-holes through the substrate."

Id. at [0102]. Thus, Glezer provides a person of ordinary skill in the art with a reason and a technique to place the contacts either facing the same direction as the sensors or the opposite way, and further taught ordinarily skilled artisans that this was mere routine design choice. A person of skill in the art working with Leader-Wang would have found it obvious to use this teaching of Glezer to modify Leader-Wang to make the contacts all face the same direction to facilitate cartridge-analyzer interface. Ex. 1020 (Crooks Decl.) at ¶ 111.

I. Dependent Claim 3 Would Have Been Obvious Over Leader-Wang, in Further View of Either Schibli or Glezer

Leader-Wang, in combination with either Schibli or Glezer, renders obvious that "the analyte sensors and the contact points of the second substrate are connected via wiring extending from the sensors through the substrate to the second surface thereof and from the second surface through the substrate to the contact points." Because claim 3 depends from claim 2, the analysis of claim 3 incorporates the analysis for claim 2, above, as well as the following.

Picking up from the analysis for claim 2, above, claim 3 adds the additional limitation on how the contact points on the second substrate (the substrate on which the sensors and contacts face the same direction) are wired. A person of ordinary skill in the art, designing the version of Leader-Wang discussed with respect to claim 2, where all contacts face the same direction, would be confronted with the problem of how to wire the contacts on the second (same-side) substrate. Ex. 1020 (Crooks Decl.) at ¶ 114. One way to do that is taught by Glezer, where the wire would run along the first surface of the second substrate, but that design requires insulation from the sample solution such as Glezer's dielectric layer. *Id.* It would have been much more obvious to simply make further use of Leader's subminiature through-hole technology and run the wire back through the second substrate to the first surface where the contact is located. *Id.* Such a design is shown below, with the path of the wiring shown in blue:

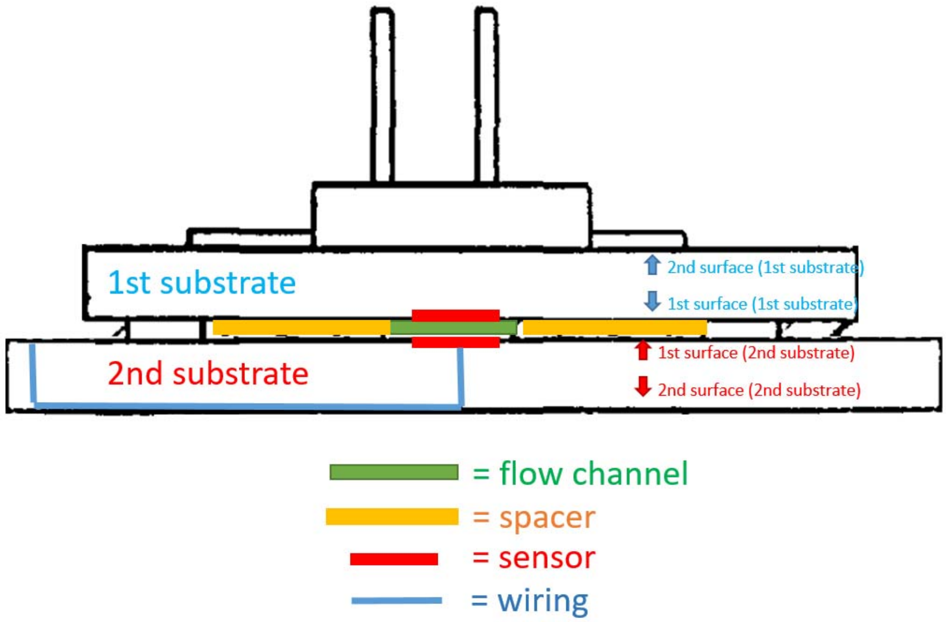


Id. This design is particularly obvious because a person of ordinary skill in the art, working with Leader, would have wanted to continue using the through-holes, consistent with Leader's innovation and design principles. *Id.* Of course, as described below, a person of ordinary skill in the art would have also found it obvious to improve the design shown above further to afford easy access to the contacts on the second substrate.

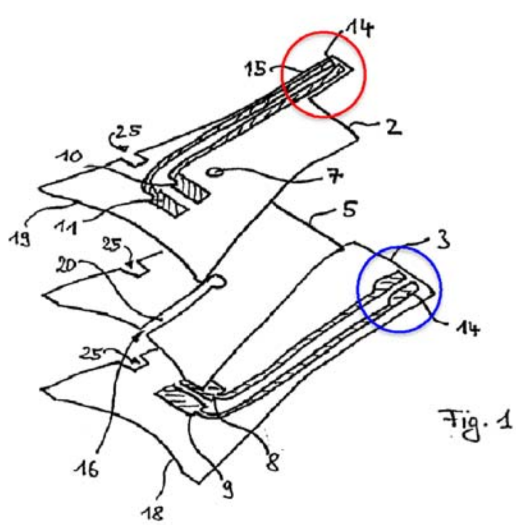
J. Dependent Claim 4 Would Have Been Obvious Over Leader-Wang, in Further View of Either Schibli or Glezer

Leader-Wang, in combination with either Schibli or Glezer, renders obvious that "a part of the second substrate extends beyond the first substrate." Because claim 4 depends from claim 3, the analysis of claim 4 incorporates the analysis for claim 3, above, as well as the following.

Continuing from the analysis for claim 3, a person of ordinary skill in the art would have sought to provide access to all the contacts on the Leader-Wang sensor assembly. In order to make all the contacts accessible to an analyzer interface, a person of ordinary skill in the art would have simply extended the second substrate beyond the first substrate, as shown:



Ex. 1020 (Crooks Decl.) at ¶ 117. Both Schibli and Glezer teach this solution to the problem of how to allow upward access to the electrical contacts on a lower substrate. *Id.* at 118. As mentioned earlier, Schibli includes a cutout on the upper layer near the numeral 2 to allow the lower contacts to avoid being blocked by the upper layer:



Ex. 1007 (Schibli) at Figure 1. Glezer also addresses the concern of ensuring that the contact pads are not block by any of the layers above them. This is shown in Figures 1c and 14b, for example, showing that the contact pads 182 are clear of the dielectric layer because the bottom substrate overhands the dielectric layer, allowing the contacts to be interfaced, with a conductive layer 1423 and ultimately the reader. Ex. 1008 (Glezer) at [0241], [0253], & Figure 23; Ex. 1020 (Crooks Decl.) at ¶ 119.

Thus, in view of either Schibli or Glezer, a person of ordinary skill in the art would have found it obvious to extend the second substrate of Leader-Wang so that it extends beyond the first substrate, to afford easy access to the contacts.

K. Dependent Claim 5 Would Have Been Obvious Over Leader-Wang, in Further View of Either Schibli or Glezer

Leader-Wang, in combination with either Schibli or Glezer, renders obvious that "the electrical contact points of the second substrate are positioned on the extending part." Because claim 5 depends from claim 4, the analysis of claim 5 incorporates the analysis for claim 4, above, as well as the following.

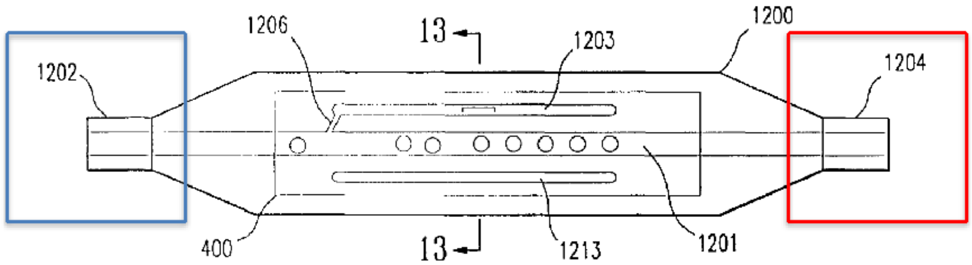
Continuing on from claim 4, claim 5 would have been obvious for all the same reasons. As explained above, the reason why a person of ordinary skill in the art would have extended the lower substrate beyond the upper substrate of Leader-Wang was precisely to allow the contacts to be positioned on the protruding portion (just as in Schibli and Glezer) so that they can be accessed by the analyzer. (Crooks Decl.) at ¶ 122. Therefore, claim 5 would also have been obvious.

L. Dependent Claim 6 Would Have Been Obvious Over Leader-Wang

Leader-Wang rendered obvious that "at least one of the substrates is made from a ceramic material." Because claim 6 depends from claim 1, the analysis of claim 6 incorporates the analysis for claim 1, above, as well as the following. Leader states that a preferable substrate material "is available from Coors Ceramic Company, Grand Junction Colo." and also that "the substrate may be any . . . ceramic . . . frit that can be used as a substantially smooth flat surface." Ex. 1003 (Leader) at 7:22-31. Thus, ceramic would have been an obvious choice for at least one substrate. Ex. 1020 (Crooks Decl.) at ¶¶ 123-25.

M. Dependent Claim 7 Would Have Been Obvious Over Leader-Wang

Leader-Wang rendered obvious that "the measuring cell has inlet and outlet ports, the ports being formed in the first substrate." Because claim 7 depends from claim 1, the analysis of claim 7 incorporates the analysis for claim 1, above, as well as the following. Leader, as shown in Figure 12, taught both inlet and outlet ports (1202 and 1204, respectively) allowing flow through the flow cell. Figure 12 is reproduced below, with the inlet in blue and outlet in red:



Ex. 1020 (Crooks Decl.) at ¶ 128. Wang, in contrast, shows its inlet and outlet formed in one of its two substrates, as shown in Figure 1 of Wang (inlet A and outlet B):

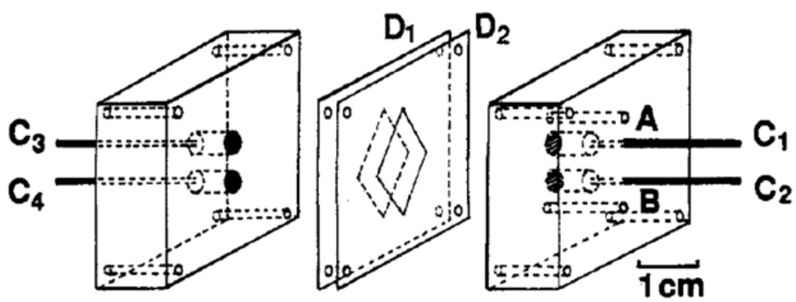


Figure 1. Expanded view of the thin-layer flow cell: (A, B) solution inlet and outlet; (C_1–C_4) working electrodes; (D_1, D_2) spacers.

Ex. 1005 (Wang) at 1925; Ex. 1020 (Crooks Decl.) at ¶¶ 129-30. In the Leader-Wang combination, it would have been obvious to adopt Wang's placement of the inlet and outlets in a substrate. Ex. 1020 (Crooks Decl.) at ¶¶ 130-31. As Dr. Crooks explains, this configuration would have allowed the use of a single, unitary spacer structure rather than one with some additional complexity that allows fluid into and out of the flow cell—just as in Wang. *Id.* at ¶ 131.

N. Dependent Claim 8 Would Have Been Obvious Over Leader-Wang

Leader-Wang taught that "the measuring cell has inlet and outlet ports, the ports being formed in the second substrate." Because claim 8 depends from claim 1, the analysis of claim 8 incorporates the analysis for claim 1, above, as well as the following. Claim 8 is identical to claim 7 except that it calls for the inlet and outlet ports to be formed in the second substrate instead of the first. Because the designation of which substrate is first and which is second is arbitrary in claim 1, claim 8 would have been obvious for the same reasons as claim 7. Ex. 1020 (Crooks Decl.) at ¶¶ 132-33.

O. Dependent Claim 9 Would Have Been Obvious Over Leader-Wang

Leader-Wang rendered obvious that "the sensor assembly is at least substantially enclosed in a housing." Because claim 9 depends from claim 1, the analysis of claim 9 incorporates the analysis for claim 1, above, as well as the following. Leader described that its sensor assembly was enclosed in a housing, e.g., a plastic encasement. Ex. 1003 (Leader) at 6:9-12. Similarly, it would have been obvious to provide Leader-Wang with a housing to provide structural integrity (holding the layers together), cleanliness, and protection for the contact wiring. Ex. 1020 (Crooks Decl.) at ¶ 136.

P. Dependent Claim 10 Would Have Been Obvious Over Leader-Wang

Leader-Wang taught that "the analyte sensors are blood parameter sensors." Because claim 10 depends from claim 1, the analysis of claim 10 incorporates the analysis for claim 1, above, as well as the following. Leader's sensors are blood parameter sensors, such as sensors for determining gas partial pressures, concentration of electrolytes, and hematocrit, and thus, the same would have been true for Leader-Wang. Ex. 1003 (Leader) at 1:5-11; *see also id.* at claim 26 ("portable blood gas and electrolyte analyzer"); Ex. 1020 (Crooks Decl.) at ¶¶ 141-42.

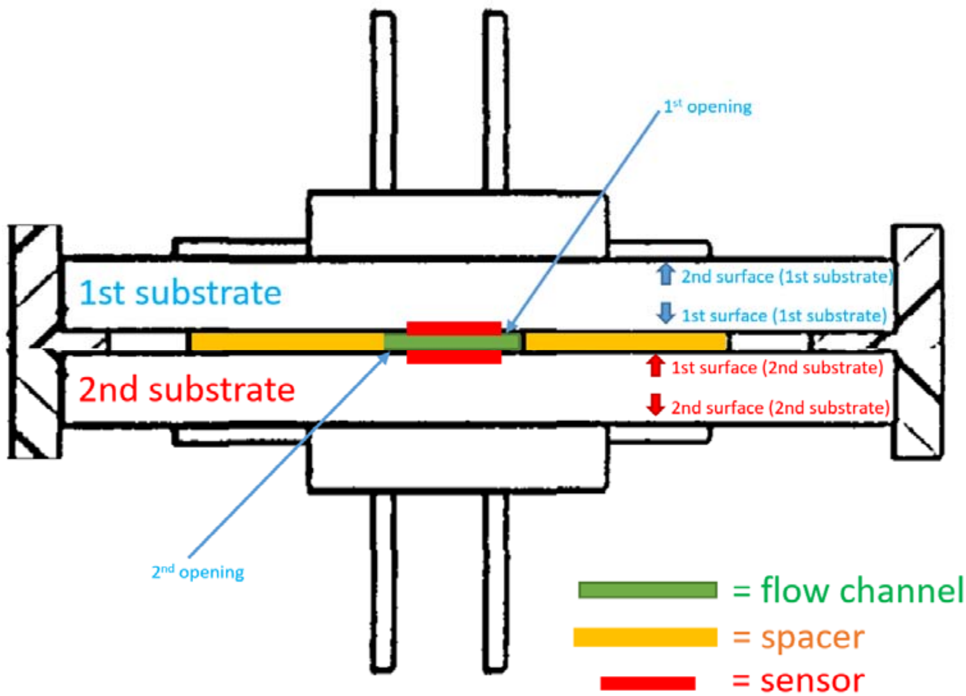
Q. Independent Claim 11 Would Have Been Obvious Over Leader-Wang

Claims 1 and 11 of the 288 patent are nearly identical. The table below shows the differences between them, highlighted in yellow.

288 patent claim 1	288 patent claim 11
The invention claimed is: 1. A sensor assembly comprising: a first electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, a second electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, and a spacer having a through-going recess with a first opening and a second opening, wherein the first substrate, the second substrate and the spacer are arranged in a layered structure, where the first surface of the first substrate closes the first opening of the spacer and the first surface of the second substrate closes the second opening of the spacer, thereby forming a measuring cell in which all the analyte sensors on the first surface of the first substrate face the measuring cell through the first opening of the spacer and wherein all the analyte sensors on the first surface of the second substrate face the measuring cell through the second opening of the spacer, the measuring cell having a shape allowing fluid flow through the measuring cell to be substantially linear.	11. A sensor assembly comprising: a first electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, a second electronic wiring substrate having a first surface and a second surface and at least two analyte sensors formed on the first surface thereof, the at least two analyte sensors being connected with electrical contact points, and a spacer having a through-going recess with a first opening and a second opening, wherein the first substrate, the second substrate and the spacer are arranged in a layered structure, wherein the first opening of the spacer is closed by the at least two analyte sensors formed on the first surface of the first substrate and by portions of the first surface of the first substrate and wherein the second opening of the spacer is closed by the at least two analyte sensors formed on the first surface of the second substrate and by portions of the second substrate, thereby forming a measuring cell in which all the analyte sensors on the first surface of the first substrate face the measuring cell through the first opening of the spacer and wherein all the analyte sensors on the first surface of the second substrate face the measuring cell through the second opening of the spacer, the measuring cell having a shape allowing fluid flow through the measuring cell to be substantially linear.

As is evident from the table above, the analysis for claim 11 is identical to the analysis for claim 1 with one small difference. Thus, the analysis for claim 11 incorporates the analysis for claim above in Section VII(G) entirely with respect to the preamble and first three limitations (Sections VII(G)(1), (2), (3), & (4)). With respect to the fourth limitation, the analysis is the same as for claim 1, Section VII(G)(5), except that claim 11 recites that the respective openings of the spacers are "closed by the at least two analyte sensors formed on the first surface of [each respective] substrate and by portions of the first surface of the [respective substrate].” Thus, the analysis for claim 11 incorporates the analysis for claim 1 in Section VII(G)(5), and adds the following.

In Leader-Wang, the openings of the spacer are closed by “the at least two analyte sensors formed on the first surface of” each substrate and “by portions of the first surface” of each substrate, as shown below:



As seen in the figure above, the openings (top and bottom of the green rectangle) are closed off by both the sensors (shown in red) and the substrate surface (which could be to the sides of the sensor or could be between the sensors in the channel direction, i.e., into and out of the page). Ex. 1020 (Crooks Decl.) at ¶ 149. This is readily observable in Figure 12 of Leader. *Id.* at ¶ 150.

Wang also taught the aspects of claim 11 that differ from claim 1. In Wang, as shown in Figure 1, the openings of the gasket layer are closed off by both the sensors and the substrate surface. Ex. 1005 (Wang) at 1925; Ex. 1020 (Crooks Decl.) at ¶ 150.

R. Dependent Claim 12 Would Have Been Obvious Over Leader-Wang

Leader-Wang taught that "the first and second openings of the spacer extend the length of a flow path defined by the measuring cell." Because claim 12 depends from claim 11, the analysis of claim 12 incorporates the analysis for claim 11, above, as well as the following. As explained in much detail above, it would have been obvious to use a spacer similar to Wang in a two-sided version of Leader. And as shown in Figure 12 of Leader, the spacer would have extended the length of the flow path, to enclose the flow path and provide access for the sensors aligned through the flow-path. Ex. 1020 (Crooks Decl.) at ¶ 155. Similarly, Wang also shows its spacer openings extending the length of the flow path from Wang's inlet to outlet. Ex. 1005 (Wang) at 1925, Figure 1; Ex. 1020 (Crooks Decl.) at ¶ 154.

S. Dependent Claim 13 Would Have Been Obvious Over Leader-Wang

Leader-Wang taught that "the first and second openings are the only openings of the spacer that define a portion of the measuring cell." Because claim

13 depends from claim 11, the analysis of claim 13 incorporates the analysis for claim 11, above, as well as the following. Claim 13 would have been obvious for the same reasons as claims 11 and 12, because Leader-Wang includes a spacer derived from Wang, with only two openings that define the measuring cell: a single opening on the top and a single opening on the bottom. Ex. 1020 (Crooks Decl.) at ¶ 158.

VIII. Conclusion

For the foregoing reasons, Petitioner has shown that there is a reasonable likelihood that the Challenged Claims of the 288 patent are unpatentable under 35 U.S.C. § 103(a). Therefore, the Board should institute a trial and cancel these claims.

Dated: December 20, 2017

Respectfully submitted,

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WORD COUNT CERTIFICATION

Pursuant to 37 C.F.R. §§ 42.24(a)(i) and 42.24(d), the undersigned certifies that the foregoing Petition for *Inter Partes* Review of U.S. Patent No. 8,728,288 contains 12,896 words as measured by the word-processing system used to prepare this paper. This word count does not include the items excluded by 37 C.F.R. § 42.24(a).

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CERTIFICATE OF SERVICE

The undersigned certifies service pursuant to 37 C.F.R. §§ 42.6(e) and 42.105(b) on the Patent Owner by Federal Express, overnight delivery, a copy of this Petition for *Inter Partes* Review and supporting materials at the correspondence address of record for the '288 patent:

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