

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIO-RAD LABORATORIES, INC.,
Petitioner,

v.

CALIFORNIA INSTITUTE OF TECHNOLOGY,
Patent Owner

Case No. IPR2024-01177

U.S. Patent No. 10,068,051 B2

PATENT OWNER PRELIMINARY RESPONSE

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EXHIBIT LIST

Exhibit No.	Description
2001	Declaration of Kevin Struhl, Ph.D.
2002	<i>Curriculum Vitae</i> of Kevin Struhl, Ph.D.
2003	File history of U.S. Patent No. 10,068,051
2004	U.S. Provisional Application No. 61/507,082
2005	Patent Scheduling Order dated March 8, 2024, Dkt No. 47, <i>ChromaCode, Inc. v. Bio-Rad Laboratories et al.</i> , Case No. 5:23-cv-06360, N.D. Cal.
2006	Petitioner's Amended Invalidity Contentions, <i>ChromaCode, Inc. v. Bio-Rad Laboratories et al.</i> , Case No. 5:23-cv-06360, N.D. Cal.
2007	Comparison of Saxonov and Saxonov Provisional
2008	Appendix A to Bio-Rad's Amended Invalidity Contentions
2009	Appendix C to Bio-Rad's Amended Invalidity Contentions
2010	Docket, <i>ChromaCode, Inc. v. Bio-Rad Laboratories et al.</i> , Case No. 5:23-cv-06360, N.D. Cal.
2011	Plaintiff's Opening Claim Construction Brief, <i>ChromaCode, Inc. v. Bio-Rad Laboratories et al.</i> , Case No. 5:23-cv-06360, N.D. Cal.
2012	Reply Claim Construction Brief, <i>ChromaCode, Inc. v. Bio-Rad Laboratories et al.</i> , Case No. 5:23-cv-06360, N.D. Cal.
2013	Notice Setting Claim Construction Hearing, Dkt. 83, <i>Chromacode Litig.</i> , Case No. 5:23-cv-04823, N.D. Cal.
2014	Joint Case Management Statement, Dkt. 80, <i>Chromacode Litig.</i> , Case No. 5:23-cv-04823, N.D. Cal.

I. INTRODUCTION

The Board should not institute IPR of claims 1-9 of U.S. Patent No. 10,068,051 (EX1001) because Petitioner has not met its burden of showing it has a reasonable likelihood of prevailing on any claim.

After years of significant investment in research and development, inventors from Patent Owner California Institute of Technology ("PO" or "Caltech") conceived of a long-sought and powerful technology for unambiguously distinguishing multiple analytes (e.g., genetic sequences) in any combination of presence or absence within a biological sample. The '051 Patent, entitled "Signal Encoding and Decoding in Multiplexed Biochemical Assays," is one of several Caltech patents that protect embodiments of this innovative technology. Petitioner Bio-Rad Laboratories, Inc. asserts the '051 Patent is unpatentable in view of U.S. Publication No. 2013/0040841 (EX1004, "Saxonov") alone or in combination with other alleged references. However, each of Petitioner's alleged invalidity grounds fails for multiple reasons.

First, Petitioner fails to establish Saxonov qualifies as prior art under 35 U.S.C. §102(e), or any other code section. Although Saxonov nominally claims priority to two provisional applications filed in July 2011 (EX1007, EX2004), Petitioner has not shown that either provisional application contains all the subject matter on which each of Petitioner's grounds relies. Not only has Petitioner failed

to carry its burden to make the required showing, but the only provisional application of Saxonov Provisional upon which Petitioner relies also does not disclose this subject matter. Instead, this subject matter, upon which each of Petitioner's grounds relies, was only first added into Saxonov's ***non-provisional*** application, which was not filed until July 12, 2012—***after*** the '051 Patent's priority date of February 3, 2012. Because each of Petitioner's grounds relies on subject matter found exclusively in Saxonov's non-provisional application, this deficiency is fatal to the Petition.

Second, even if, *arguendo*, Saxonov were considered §102(e) prior art (it is not), Petitioner fails to show a reasonable likelihood of demonstrating that Saxonov, alone or in combination with U.S. Patent Application Publication Nos. 2008/0124705 (Kramer) and 2011/02500597 (Larson), and other ground references, renders the challenged claims unpatentable. As explained below, Saxonov is deficient in multiple regards which extend beyond its inability to claim a priority date preceding the '051 Patent's. Despite—or perhaps because of—Saxonov's deficiencies, Petitioner attempts to revise and reinterpret Saxonov in a manner which is inconsistent with Saxonov's own teachings. And, while Petitioner tries combining Saxonov with Kramer or Larson to obtain the method recited in claim 1, these references also expressly teach away from Petitioner's proposals.

In view of the Petition's substantial deficiencies, Petitioner has failed to demonstrate a reasonable likelihood of prevailing on any claim. The Petition should be denied. Alternatively, the Board should exercise its discretion to deny institution because the *Fintiv* factors as a whole weigh in favor of denial.

II. BACKGROUND

A. Technology

A variety of techniques have been developed to detect a target polynucleotide analyte, such as a particular genetic sequence, within a biological sample. EX2001, ¶28. Caltech's innovations described and claimed in the '051 Patent and its priority applications addressed a long-standing problem in the field: namely, as the number of analytes in a biological sample increases, it quickly becomes more complicated to identify the analytes. EX2001, ¶29. The term "multiplexing" refers to a broad class of techniques for detecting multiple analytes in a biological sample. *Id.* Early assays used polymerase chain reaction (PCR) to amplify (create copies of) each of the target polynucleotide analytes, and often involved gel electrophoresis to separate the various PCR products that distinguished the analytes. *Id.*

A subsequent multiplex PCR approach uses "probes" to bind to target analytes and fluoresce with different colorimetric labels (fluorophores) corresponding to the different analytes, with results being detected with

appropriate optical channels. EX2001, ¶30. For example, a probe is designed to be complementary to a particular genetic sequence, and the probe and sequence bind via “hybridization.” *Id.* The fluorophore emits light only if the probe has bound its target within the sample. *Id.* For example, a probe with a blue fluorophore binds analyte A and its light is observed in a blue channel; and a probe with a red fluorophore binds analyte B and its light is observed in a red channel. *Id.*, ¶31. Of course, increasing the numbers of probe types (each with distinct fluorophore color) and channels (one per color) increases the number of detectable analytes. *Id.* However, scaling up to detect more analytes in the same sample has the limitation of the number of distinct colorimetric probes and optical channels that could be assayed simultaneously. *Id.*

Some multiplexing techniques use probes with colorimetric labels (fluorophores) of the same color. EX2001, ¶32. Here, color alone does not distinguish the analytes from one another: light in the channel means an analyte is present, but does not identify **which** analyte is present. *Id.* Some techniques (e.g., Larson) tried to avoid this problem by (i) highly diluting the sample, (ii) physically dividing the diluted sample into droplets, (iii) observing the intensity of light from each droplet, and (iv) drawing conclusions about the analytes based on that intensity. *Id.* For example, probes with the same color could be designed to fluoresce at different intensities, to identify the analyte using the intensity. *Id.*

When a dilute sample is divided into droplets, different droplets may contain different numbers of unique analyte molecules. EX2001, ¶33. The “Poisson distribution” describes the statistics of how many analyte molecules the droplets contain. *Id.* In the “limiting dilution” regime, the majority of droplets contain zero analyte molecules, fewer droplets contain exactly one analyte molecule, even fewer contain exactly two analyte molecules, still fewer contain exactly three analyte molecules, and so on. *Id.* At terminal dilution, the sample is sufficiently diluted that the Poisson distribution basically guarantees that almost all droplets are either empty or contain only a single analyte molecule, with droplets rarely containing multiple analyte molecules. *Id.* At terminal dilution, to best avoid droplets containing multiple analyte molecules, most droplets are empty, which wastes material and time. *Id.*

The '051 Patent refers to analytes that are indistinguishable from one another in a given assay as being “degenerate.” EX1001, 17:62-65. At the time the '051 Patent and its priority applications were filed, a significant need remained for inexpensive, material-efficient, and time-efficient multiplexing that could non-degenerately identify a higher number of targets within a given sample, without the need to add another optical channel corresponding to each additional analyte. *Id.*, 1:30-42, 8:40-57; EX2001, ¶34.

B. The '051 Patent and the Challenged Claims

To address the above-described needs, Caltech inventors conceived of a solution—described and claimed in the '051 Patent and its priority applications—that enables non-degenerate detection of at least seven polynucleotide analytes, in a single sample solution volume, in any combination of presence or absence. The application that issued as the '051 Patent was filed on August 5, 2014 as a continuation of application no. 13/756,760, filed February 1, 2013. EX1001, §§(22), (63). The '051 Patent claims priority to provisional application nos. 61/594,480, filed February 3, 2012, and 61/703,093, filed September 19, 2012. EX1001, §(60).

The Caltech inventors recognized that in traditional multi-channel methods such as those described above, “the number of detectable analytes is equal to the number of spectrally resolvable fluorophores. Therefore the number of analytes may only be increased by increasing the number of spectrally resolvable fluorophores.” EX1001, 12:31-37. To overcome this limitation, the inventors developed a technique to non-degenerately identify analytes in a sample, using *fewer* fluorophores than the number of analytes (in contrast to prior multi-channel techniques). EX1001, 8:40-61. Instead, “each analyte to be detected is encoded as a value in each of two components of a signal (e.g., intensity and wavelength).” *Id.*, 8:61-67. These components are cumulatively measured for the sample, and the

“presence or absence of an analyte may then be determined based on the values used to encode the presence of the analyte (i.e., those values in the coding scheme).” *Id.*, 9:36-42.

Table 3 of the '051 Patent, below, describes an example in which seven analytes (A-G), plus control, are encoded using combinations of four fluorophores (fewer fluorophores than analytes):

TABLE 3

Encoding of eight analytes (including control) with four colors and up to four colors per analyte.				
	Blue	Green	Yellow	Red
Ctrl. (p)	1	0	0	0
A	1	0	0	1
B	1	0	1	0
C	1	1	0	0
D	1	0	1	1
E	1	1	0	1
F	1	1	1	0
G	1	1	1	1

EX1001, 14:4-15.

As the '051 Patent explains,

The presence of the control and analyte A is indicated by a result of 2001. The presence of the control and analyte G is indicated by a result of 2111. These results express the cumulative intensity of the signal in each color. For

example, the result 2111 has a 2X signal intensity in the blue channel, while the result 1000 has only a 1 X signal intensity in the blue channel. EX1001, 14:23-28.

While these example results are for a single analyte, the '051 Patent also explains how the inventive coding method may be used to detect **combinations** of different analytes in a single sample volume. For example, the following excerpt from Table 4 demonstrates that the cumulative signal intensity from the combination of analytes A-F in a single sample volume is different, and measurably distinguishable from, that from the combination of analytes A-G in a single sample volume:

TABLE 4-continued

Decoding matrix for encoding method presented in Table 3.				
Cumulative Assay Result				
Blue	Green	Yellow	Red	Analyte(s) Present
7	3	3	3	pABCDEF
8	4	4	4	pABCDEFG

EX1001, 17:1-6.

The Caltech inventors recognized that sometimes, a result may be degenerate “because it can indicate more than one possibility in terms of the presence or absence of an analyte. For example, with reference to Table 4, result 5233 is degenerate because it can be decoded as either pADFG or pBDEG.”

EX1001, 17:64-67. The Caltech solved this problem by reducing or eliminating degeneracy from the coding scheme, “thereby increasing the confidence with which an analyte is detected.” *Id.*, 18:16-18. The '051 Patent describes different ways to eliminate degeneracy, such as encoding individual analyte states using intensity levels separated by integer $\log_2$ intensity values (1, 2, 4, 8, 16, etc.) so every possible combination of analytes has a unique cumulative intensity.

EX1001, 23:33-25:19. The '051 Patent claims are directed to the Caltech inventors' innovations allowing detection of “at least seven polynucleotide analytes, in any combination of presence or absence, in a single sample solution volume.”

C. The '051 Patent's Prosecution History

Initially, Examiner Negin rejected the claims as being subject-matter ineligible, anticipated by U.S. 2003/0148544 (“Nie”), obvious over Nie in view of secondary references, or indefinite. EX2003, 2134-2147. Following PO's response including amendments and arguments, Examiner Negin issued a Final Office Action maintaining the subject-matter eligibility rejections, newly rejecting the claims as anticipated by U.S. 2013/0261019 (“Lin”) or obvious over Lin in view of secondary references, and adding an obviousness-type double patenting rejection over U.S. 8,838,394 (the '051 Patent's parent). EX2003, 2337-2353. In response, PO replied on an after-final basis with amendments, arguments, a terminal

disclaimer, and an AFCP 2.0 request. EX2003, 2363-2390. PO discussed various proposed claim amendments with Examiner Negin. EX2003, 2401-2406, 2420-2424. PO then filed an RCE and amended the independent claim as follows, into its now-granted form:

49. **(Currently Amended)** A method of detecting the presence or absence of at least seven polynucleotide~~each~~ analytes, in any combination of presence or absence, in a single sample solution volume ~~of a plurality of analytes~~, the method comprising:

~~a)[a.] encoding each of said analytes as a first value of a signal, thereby generating a coding scheme, wherein each of said analytes is represented in said coding scheme by one of said first values, wherein said encoding is performed in a manner that reduces or eliminates degeneracy;~~

~~a)[b.] providing a sample solution volume comprising, or potentially comprising, at least one of said at least seven polynucleotide analytes, and comprising at least seven hybridization probes, each hybridization probe corresponding to one of the at least seven polynucleotide analytes, wherein each hybridization probe comprises at least one fluorophore selected from four fluorophores, and wherein each hybridization probe, when excited~~

and when contacted with its corresponding polynucleotide analyte, generates a cumulative intensity signal, further wherein each generated cumulative intensity signal comprises at least one signal generated by excitement of at least one of the four fluorophores;

b)[[c.]] contacting said sample solution volume with the plurality of hybridization probes and exciting the hybridization probes to generate the cumulative intensity signal(s) if one or more of the at least seven polynucleotide analytes is present in the sample volume; analyte-specific reagents that generate said first value, as represented in said coding scheme, when each of said analytes is present; and

c)[[d.]] measuring the cumulative intensity signal(s), thereby generating a cumulative signal measurement, wherein the cumulative signal measurement non-degenerately indicates the presence or absence of the at least seven polynucleotide analytes, in any combination of presence or absence, cumulatively measuring said first values of said signal within said sample, thereby providing a cumulative measurement;

~~e)[[e.]] determining whether each of said analytes is present or absent based on said cumulative measurement and said coding scheme;~~

wherein said method non-degenerately detects the presence or absence of the at least seven polynucleotide analytes in ~~[[a]]~~said single sample solution volume, in any combination of presence or absence, without requiring any step of immobilization of said polynucleotide analytes, physical separation of said polynucleotide analytes, or mass ~~spectometry~~spectrometry.

EX2003, 2441-2442.

Subsequently, PO filed an IDS citing Saxonov, which Examiner Negin initialed to indicate that he considered Saxonov. EX2003, 2566, 2675. PO had also cited Kramer in an earlier IDS, which Examiner Negin also initialed to indicate he considered Kramer. EX2003, 1893, 2191.

Examiner Negin then allowed the application, stating “[t]he claims recite a new and non-obvious assay to detect the presence/absence pattern of seven different analytes using non-degenerate hybridization techniques.” EX2003, 2658.

Examiner Negin also examined Saxonov around the same time as the '051 Patent's family. *See generally* EX2003; EX1004.

D. The Ground References

Each of Petitioner's grounds relies on Saxonov as the primary reference. See Petition at 29-67. As described in §V.A., Petitioner does not (and cannot) establish Saxonov as §102(e) prior art against the '051 Patent for the grounds set forth in the Petition. Moreover, as described below in §V.B., Petitioner fails to establish that the claims are unpatentable over Saxonov, whether alone or in combination with the other ground references.

1. Saxonov

Saxonov was filed July 12, 2012 and claims priority to U.S. Provisional Patent App. Nos. 61/507,082, filed July 12, 2011, and 61/510,013, filed July 20, 2011 ("Saxonov Provisional"). EX1004, §§(22), (60).

Saxonov discloses "performing a digital assay with multiplexed detection of two or more distinct targets in the same optical channel." EX1004, Abstract.

Regarding "digital assays," Saxonov explains:

Digital assays generally rely on the ability to detect the presence or activity of individual copies of an analyte in a sample. In an exemplary digital assay, a sample is separated into a set of partitions, generally of equal volume, with each containing, on average, less than about one copy of the analyte. If the copies of the analyte are distributed randomly among the partitions, some partitions should contain no copies, others only one copy,

and, if the number of partitions is large enough, still others should contain two copies, three copies, and even higher numbers of copies. The probability of finding exactly 0, 1, 2, 3, or more copies in a partition, based on a given average concentration of analyte in the partitions, is described by a Poisson distribution.

EX1004, ¶3.

Here, Saxonov teaches that in a standard digital assay, most droplets (partitions) are empty, fewer droplets contain exactly one analyte, even fewer contain exactly two analytes, and even fewer contain exactly three analytes; this is consistent with the limiting dilution regime discussed above in §II.A. EX2001, ¶52.

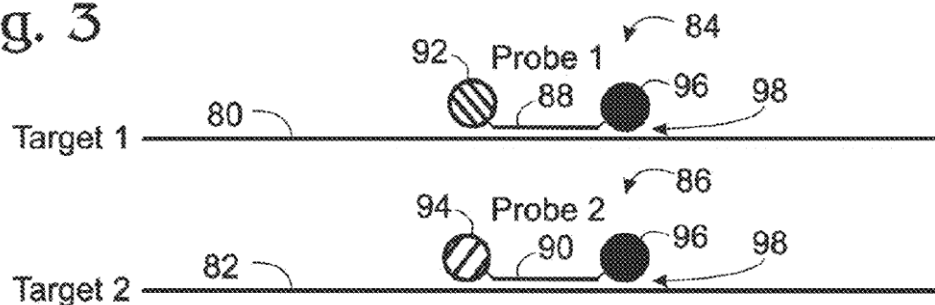
According to Saxonov, “[d]igital assays frequently rely on amplification of a nucleic acid target in partitions to enable detection of a single copy of an analyte,” and such “[a]mplification may be conducted via the polymerase chain reaction (PCR).” EX1004, ¶5. Saxonov states “[a]mplification of the target can be detected optically from a fluorescent probe included in the reaction,” and “the probe can include a dye that provides a fluorescence signal indicating whether or not the target has been amplified.” *Id.*

Like others, Saxonov tried to multiplex: “[a] new approach is needed to increase the multiplex levels of digital assays.” EX1004, ¶7. Saxonov identified

various shortcomings in then-known multiplexing techniques, such as “instruments with more optical channels, to detect emission from more dyes, are more expensive than those with fewer channels,” and “increasing the number of distinguishable dyes is expensive and becomes impractical beyond a certain number.” *Id.*, ¶6.

Saxonov tried solving this problem using a “common or shared channel (‘the same optical channel’)” to detect signals from “reporters for two or more distinct targets.” EX1004, ¶19. For example, in FIG. 3, Saxonov illustrates target sequences 80, 82; probes 84, 86 with oligonucleotides 88, 90; and fluorophores 92, 94; when oligonucleotide 88 hybridizes to sequence 80 or oligonucleotide 90 hybridizes to sequence 82, the respective fluorophores separate from quenchers 96 and fluoresce. *Id.*, ¶¶48-52.

Fig. 3



Saxonov describes different ways to distinguish the fluorophores' signals based on intensity, including that “one probe may be labeled with a different number of fluorophores than the other probe,” or “there may be less of one probe than the other in the sample,” or “the fluorophores themselves might be different,

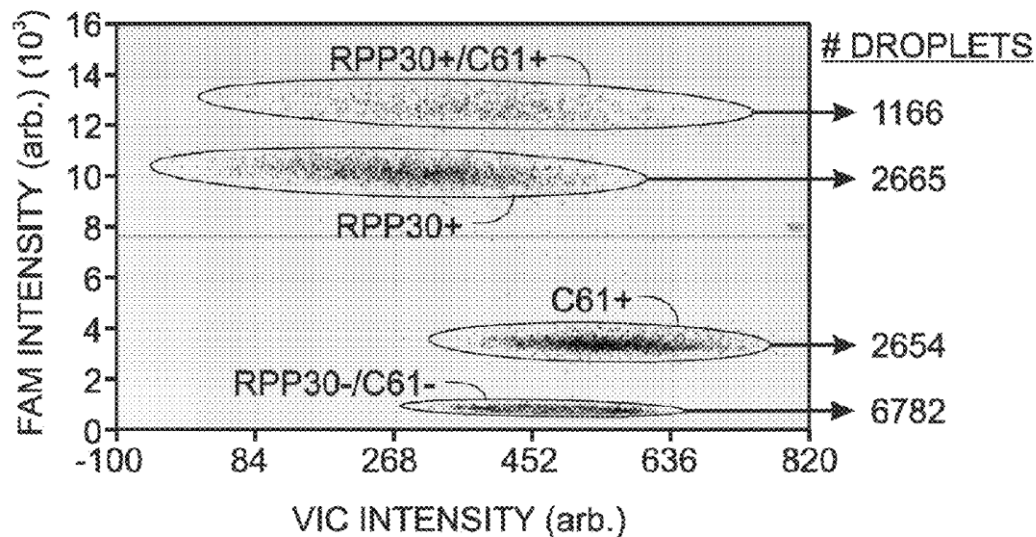
with one more or less intrinsically fluorescent than the other.” EX1004, ¶51.

According to Saxonov, the partition “may be classified as being positive or negative for each of the reactions/targets contributing to the signal.” *Id.*, ¶41.

Saxonov states the “data including all permutations of positives will generally fall into 2^N populations or clusters, where N is the number of targets, assuming that each population is distinguishable.” EX1004, ¶41.

Saxonov FIG. 5 illustrates clusters for a two-analyte system (assaying the C61 and RPP30 genes) in a common channel (the channel for FAM, a fluorophore type). EX1004, ¶¶51, 60, 63; EX2001, ¶58.

Fig. 5



In FIG. 5, the RPP30-/C61- cluster of 6782 droplets “corresponds to droplets that are negative for RPP30 and C61 (i.e., droplets that did not include either gene).” EX1004, ¶64. The C61+ cluster of 2654 droplets “corresponds to droplets

that are positive for C61 and negative for RPP30 (i.e., droplets that included the C61 gene but did not include the RPP30 gene).” *Id.*, ¶65. The RPP30+ cluster of 2665 droplets “corresponds to droplets that are positive for RPP30 and negative for C61 (i.e., droplets that included the RPP30 gene but did not include the C61 gene).” *Id.*, ¶66. The RPP30+/C61+ cluster of 1166 droplets “corresponds to droplets that are positive for both RPP30 and C61 (i.e., droplets that included both genes).” *Id.*, ¶67.

FIG. 5 is consistent with Saxonov’s digital assay description above and with the “limiting dilution” regime (*supra* §II.A.): 6782 droplets were empty (the majority); 2654+2665=5319 droplets contained a single analyte (fewer than the number of empty droplets); and 1166 droplets contained both analytes (fewer than the number containing a single analyte). EX2001, ¶60.

Saxonov’s FIG. 5 is fairly simple because there are only two analytes and four populations or clusters. EX2001, ¶62. According to Saxonov, as the number of targets (N) increases, the number of clusters increases as 2^N . EX1004, ¶41; EX2001, ¶¶57, 62. Using the tables below, Saxonov shows a single target A (N=1) yields two clusters ($2^1=2$); two targets A and B (N=2) yield four clusters ($2^2=4$), and three targets A, B, and C (N=3) yields eight clusters ($2^3=8$). EX1004, ¶41, EX2001, ¶62.

	Target A	Intensity
Population 2	+	Highest
Population 1	–	Lowest

	Target A	Target B	Intensity
Population 4	+	+	Highest
Population 3	+	–	Intermediate
Population 2	–	+	Intermediate
Population 1	–	–	Lowest

	Target A	Target B	Target C	Intensity
Population 8	+	+	+	Highest
Population 7	+	+	–	Intermediate
Population 6	+	–	+	Intermediate
Population 5	–	+	+	Intermediate
Population 4	+	–	–	Intermediate
Population 3	–	+	–	Intermediate
Population 2	–	–	+	Intermediate
Population 1	–	–	–	Lowest

EX1004, ¶41.

As explained below in §V.A.5., Saxonov's FIGS. 9 and 10 and ¶¶17, 18, and 76-79 were only added on Saxonov's non-provisional filing date and thus are not prior art to the '051 Patent. Nonetheless, Petitioner relies on this subject matter and it is, therefore, briefly discussed below.

According to Saxonov, FIG. 9 is:

a schematic representation of an exemplary bulk phase mixture being separated into droplets during performance of an exemplary digital assay with multiplexed detection of three or more distinct targets (T1, T2, and T3) using a reporter for each target (a T1 probe, a T2 probe, and a T3 probe) each including a different luminophore (L1, L2, and L3, respectively). EX1004, ¶17.

Fig. 9

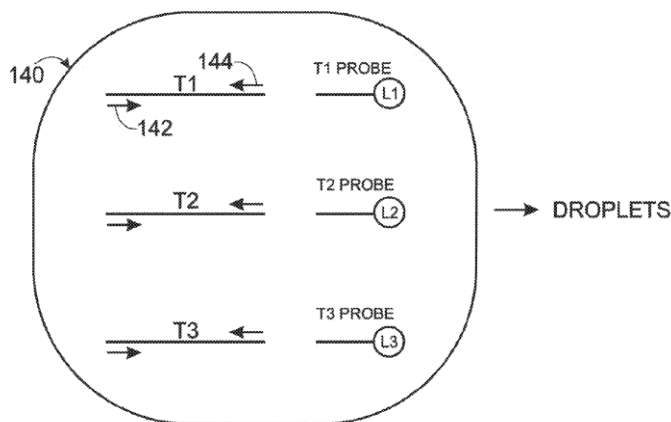


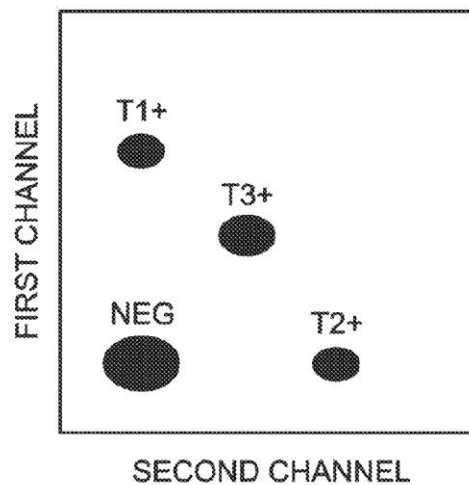
FIG. 9 shows that the volume containing the three targets T1, T2, T3 and corresponding probes is divided into droplets. EX2001, ¶65.

According to Saxonov, FIG. 10:

is a schematic representation of an exemplary graph showing droplet (or peak) intensities for a T1/T2/T3 droplet assay that may be performed with the droplets of FIG. 9, where data from the T1, T2, and T3 probes are collected in a first optical channel and a second optical

channel and plotted as a function of intensity in the first channel (vertical axis) versus intensity in the second channel (horizontal axis), with intensities produced by exemplary populations or clusters of negative (NEG), T1-positive (T1+), T2-positive (T2+), and T3-positive (T3+) droplets represented by filled ellipses[.] EX1004, ¶18.

Fig. 10



Saxonov states that in FIG. 10, “[t]o simplify the presentation, double-positive populations (T1+/T2+, T1+/T3+, and T2+/T3+) and the triple-positive population are **not shown**,” but alleges that “the populations containing more than one target may be resolved and distinguishable from one another and from the single-target populations and the negative population.” EX1004, ¶¶78-79.

Examiner Negin examined the '051 Patent around the same time that he examined Saxonov. *See generally* EX2003; EX1004.

2. Kramer

U.S. Patent Application Publication No. 2008/0124705 to Kramer (“Kramer”) was filed on April 30, 2003, and issued on May 29, 2008. EX1008, §§(22), (43).

The Petition alleges that Saxonov, combined with Kramer, renders obvious certain claims of the '051 Patent. Petition, 55 et seq.

Kramer discloses “[h]ighly multiplexed homogeneous in vitro screening assays for numerous possible nucleic acid targets, any of which might be present in a sample.” EX1008, Abstract. According to Kramer, “homogeneous” means “nucleic acid targets are detected in solution without segregating targets spatially and without washing away hybridization probes.” *Id.*, ¶9. Kramer discloses that its multiplexing uses:

combinatorial coding, with or preferably without added ratio coding, utilizing a panel of distinguishable fluorophores. In a combinatorial code, each code element is identified by its unique pattern of different labels, in this case colors. The combinatorial code includes up to four different fluorophores per code element. EX1008, ¶11.

Kramer contemplates using “ratio coding” to supplement combinatorial coding in “screening assays in which it is highly likely that only one target will be found[.]” EX1008, ¶11; EX2001, ¶72. Kramer teaches that “assays that are not

highly likely to find only one target” use “strictly combinational coding.”

EX1008, ¶32.

3. Larson

U.S. Patent Application Publication No. US 2011/0250597 to Larson et al. (“Larson”) was filed on February 11, 2011, and issued on October 13, 2011.

EX1017, §§(22), (43).

Petitioner alleges Saxonov, combined with Larson, renders obvious certain claims of the '051 Patent. Petition, 55 et seq.

Larson discloses “droplet based digital PCR and methods for analyzing a target nucleic acid using the same.” EX1017, Abstract. Larson states that it is “based on the singular nature of amplifications at terminal or limiting dilution that arises because most often only a single target allele is ever present in any one droplet even when multiple primers/probes targeting different alleles are present.” *Id.*, ¶¶45, 98, 99. Larson describes terminal dilution as “the vast majority of reactions contain either one or zero target DNA molecules for practical intents and purposes,” and limiting dilution as “some reactions contain zero DNA molecules, some reactions contain one molecule, and frequently some other reactions contain multiple molecules, following the Poisson distribution.” EX1017, ¶6. Larson asserts various advantages of having one allele per droplet. *See, e.g., id.*, ¶¶99-100.

Larson discloses digital PCR (dPCR) assays for detecting different numbers of analytes; illustratively, FIG. 15 discloses a “9-plex dPCR assay for spinal muscular atrophy with only two fluorophores, showing the process of optimizing droplet intensities.” EX1017, ¶35.

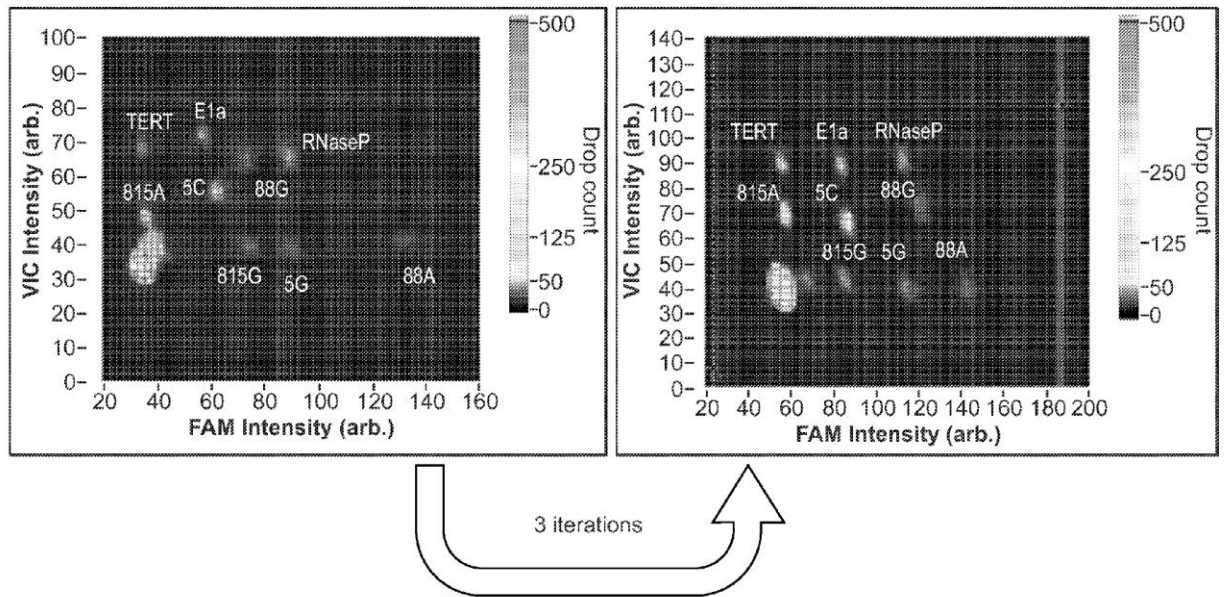


FIG. 15

Like FIG. 10 of Saxonov, Larson’s FIG. 15 shows only single-analyte clusters (respectively TERT, 815A, E1a, 5C, 815G, RNaseP, 88G, 5G, 88A). EX1017, ¶35, FIG. 15; EX2001, ¶78.

Larson teaches “[h]igher degrees of multiplexing would require greater dilution,” because of the possibility for unintended “cross-reactivity” between analytes in a given droplet. EX1017, ¶129. Accordingly, Larson teaches increasing the sample dilution as the number of analytes increases, in order to

reduce the probability that any droplet contains even two analytes, let alone more than two. EX2001, ¶¶79-84.

E. Related Proceedings

The '051 Patent is the subject of ongoing litigation between PO and Petitioner. On October 5, 2023, ChromaCode, Inc.—the exclusive licensee of the '051 Patent—filed an infringement lawsuit against Petitioner in the Central District of California. *ChromaCode, Inc. v. Bio-Rad Labs., Inc.*, No. 2:23-cv-08417 (C.D. Cal.). On October 13, 2023, ChromaCode filed an Amended Complaint, which PO joined as a plaintiff. *Id.*, Dkt. 12 (EX1028). The case was transferred to the Northern District of California and consolidated with another action by ChromaCode seeking declaratory judgment of non-infringement of certain of Petitioner's patents. *See In re: ChromaCode Litig.*, No. 5:23-cv-04823 (N.D. Cal.), Dkts. 71, 73; *ChromaCode, Inc. v. Bio-Rad Labs., Inc.*, No. 5:23-cv-06360 (N.D. Cal.) (“the parallel litigation”), Dkt. 77, 78. The consolidated litigation is pending before Judge Eumi K. Lee.

On March 8, 2024, a Scheduling Order issued in the parallel litigation outlining deadlines for contentions, claim construction briefing, and discovery. EX2005. Pursuant to the order, ChromaCode and PO served infringement contentions on March 21, 2024.

PO and ChromaCode filed a Second Amended Complaint on March 27, 2024. *ChromaCode v. Bio-Rad*, No. 5:23-cv-06360, Dkt. 54. The case schedule was amended to accommodate the Second Amended Complaint. *Id.*, Dkt. 53 (EX1027). Petitioner and PO served damages contentions and responses between March 29, 2024 and August 1, 2024. Petitioner served invalidity contentions on May 13, 2024, which Petitioner amended on June 17, 2024. EX2006. Petitioner's contentions include invalidity grounds based on Saxonov, Kramer, and/or Larson for claims 1-4, and include additional references such as Silverbrook, Maltezos, and Oh for claims 5-9. EX2006, 7-12. These references are asserted here in grounds 1-8.

On June 24, 2024, the court entered an ESI order. *ChromaCode v. Bio-Rad*, No. 5:23-cv-06360, Dkt. 67. The parties completed *Markman* briefing on August 9, 2024. EX1027; *see also* EX2010, 11. A claim construction tutorial is scheduled for December 3, 2024 and a *Markman* hearing is scheduled for December 12, 2024. EX2013. Fact discovery is well under way. Under the current scheduling order, fact discovery is set to close on November 1, 2024 and expert discovery is set to close on February 20, 2025. EX1027. The court will be holding a scheduling conference on November 6, 2024 and PO expects the court will set a deadline for the close of fact discovery within a few months of the *Markman* order. *See ChromaCode Litig.*, No. 5:23-cv-04823, Dkt. 82.

III. PERSON OF ORDINARY SKILL IN THE ART

For purposes of this IPR proceeding, PO does not contest Petitioner's description of qualifications for a person of ordinary skill in the art (POSA) set forth at Petition, 10-11.

IV. CLAIM CONSTRUCTION

Petitioner "requests that the Board understand the claims consistent with the apparent interpretations that [PO] is pursuing in the parallel litigation[.]" Petition, 27-28. PO agrees. The Board should adopt PO's proposed constructions from the parallel litigation as follows:

Claim Terms	PO's Proposed Construction	Support
"providing a sample solution volume . . . comprising at least seven hybridization probes" and "contacting. . ." '051 Patent Claim 1.	Not indefinite; plain and ordinary meaning	EX1003, 6-9 EX2011, 25-27 EX2012, 6-10
"non-degenerately," "degenerate" or "degeneracy" '051 Patent Claim 1.	Plain and ordinary meaning	EX1003, 9-11 EX2011, 27-28 EX2012, 18-19
"each [of said at least 7] hybridization probe[s]" '051 Patent Claim 1.	Plain and ordinary meaning	EX1003, 11-13 EX2011, 14-15 EX2012, 16-18

Claim Terms	PO's Proposed Construction	Support
“cumulative intensity signal(s)” '051 Patent Claims 1, 4.	Plain and ordinary meaning. To the extent a construction is necessary, “signal representing the total intensity of the light emitted by a given probe”	EX1003, 14-16 EX2011, 17-18 EX2012, 14-15
“cumulative [signal/intensity] measurement” '051 Patent Claim 1.	“measurement of the cumulative intensity signal(s) in the volume”	EX1003, 16-18 EX2011, 19-21 EX2012, 15-16
“single sample solution volume” '051 Patent Claim 1.	Limiting; plain and ordinary meaning	EX1003, 19-21 EX2011, 10-14 EX2012, 12-14
“wherein said method non-degenerately detects the presence or absence of the at least seven polynucleotide analytes in said single sample solution volume, in any combination of presence or absence” '051 Patent Claim 1.	Limiting; plain and ordinary meaning	EX1003, 23-26 EX2011, 10-14 EX2012, 12-14

V. THE BOARD SHOULD DENY INSTITUTION

A. Saxonov Is Not Prior Art

Petitioner alleges that certain subject matter within Saxonov renders the challenged claims unpatentable. However, while the two provisional applications to which Saxonov nominally claims priority were filed before the '051 Patent's earliest priority application, the provisional application upon which the Petitioner relies (the Saxonov Provisional) does not actually disclose all of the relied-upon subject matter. Instead, certain relied-upon subject matter was newly added when Saxonov was converted to a non-provisional, and is found **only** in the Saxonov non-provisional. Thus, for purposes of the grounds advanced in the Petition, Saxonov is entitled only to its **non-provisional** filing date of July 12, 2012—**after** the '051 Patent's earliest priority date of February 3, 2012. Because each of Petitioner's grounds relies on the later-added subject matter (which is not prior art), the Board should deny institution.

1. Petitioner's Position on the '051 Patent and Saxonov

Petitioner expressly assumes the '051 Patent's priority claim to February 3, 2012: "For purposes of only this proceeding, it is assumed herein that the '051 patent is entitled to a February 3, 2012, priority date." Petition, 6. This priority date is **before** Saxonov's non-provisional filing date of July 12, 2012, so Petitioner relies on the earlier filing date of the Saxonov Provisional, arguing "Saxonov is

§102(e) prior art as of at least the filing of the [Saxonov] provisional, July 20, 2011, because the [Saxonov] provisional supports Saxonov's method of performing a digital assay recited in its claim 1." *Id.*, 11.

2. By Assuming the '051 Patent Is Entitled to Its Earliest-Claimed Priority Date, Petitioner Has Failed to Shift the Burden to Patent Owner to Prove this Entitlement

"The Board cannot adopt arguments on behalf of Petitioner; 'the Board must base its decision on arguments that were advanced by a party.'" *Apple Inc. v. Telefonaktiebolaget LM Ericsson*, IPR2022-00348, Paper 9 at 4 n.2 (PTAB Sept. 21, 2022) (quoting *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016)). Here, Petitioner has not asserted (or even hinted) that the '051 Patent is not entitled to its February 3, 2012 priority date. To the contrary, Petitioner **explicitly assumes** the '051 Patent is entitled to this priority date. Petition at 6. Thus, Petitioner has not shifted the burden of production to PO to prove the '051 Patent is entitled to its February 3, 2012 priority date.

The Board's decision in *Ariosa Diagnostics, Inc. v. Illumina, Inc.* is instructive regarding Petitioner's failure to shift its burden on this issue. See IPR2014-01093, Paper 69 (PTAB Jan. 7, 2016). There, the challenged '794 patent claimed priority to an application filed before the filing date of petitioner's "prior art" reference—Fan. *Id.*, 3, 5. Fan, though, claimed priority to provisional applications filed before the '794 patent's priority claim. *Id.*, 5-6. The patent

owner argued Fan was not prior art because it was not entitled to priority back to its listed provisional applications, that it was petitioner's burden to establish Fan was prior art, and that petitioner did not meet that burden. *Id.*, 7. Additionally, the patent owner argued that petitioner acknowledged the '794 patent's priority claim and did not attempt to demonstrate that the '794 patent was not entitled to that priority date. *Id.*

The *Ariosa* petitioner argued it satisfied its burden to show Fan was prior art by stating Fan was prior art and noting the '794 patent's filing date (which was before Fan's filing date). *Ariosa*, IPR2014-01093, Paper 69 at 12. The petitioner asserted that this shifted the burden to the patent owner to demonstrate the '794 patent was entitled to an earlier priority date (its provisional), which the patent owner purportedly failed to do. *Id.*

In holding that petitioner **failed** to show Fan was prior art, the Board noted “there was **no argument** in the Petition that the '794 patent was not entitled to its earliest possible effective filing date....” *Ariosa*, IPR2014-01093, Paper 69 at 13.¹ Thus, the Board found “a fair reading of the Petition would have put Patent Owner on notice, **at best**, that Petitioner was relying on the Fan application with an effective filling date of the [Fan] provisional; but **not** as putting Patent Owner on

¹ Emphasis added throughout except where noted.

notice that Petitioner was contending that the '794 patent was not entitled to priority back to" its provisional filings. *Id.*, 13-14. "Specifically, as Petitioner...**never argued** that the '794 patent was not entitled to its earliest effective filing date, it did **not** shift the burden of production to [PO] to demonstrate that the '794 patent was entitled to its earliest effective filing date." *Id.*, 14.

Ariosa is squarely on point. Here, Petitioner similarly has not argued the '051 Patent is not entitled to its provisional priority date of February 3, 2012, but instead **assumes** the '051 Patent **is** entitled to that priority date. Thus—just as in *Ariosa*—Petitioner has not shifted the burden to PO to demonstrate the '051 Patent is entitled to the February 3, 2012 priority date, which pre-dates Saxonov's July 12, 2012 filing date.

3. It Was Petitioner's Burden to Show the Relied-Upon Subject Matter from Saxonov Was Carried Over from the Saxonov Provisional

"In an [IPR], 'the petitioner is master of its complaint,' and 'the petition [is] the center-piece of the proceeding.'" *Telefonaktiebolaget*, IPR2022-00348, Paper 9 at 4 (quoting *SAS Inst., Inc., v. Iancu*, 138 S. Ct. 1348, 1355, 1359 (2020)). "[A] petitioner carries a burden of production to show in its petition that the asserted references qualify as prior art." *Id.* (citing *Dynamic Drinkware, LLC v. Nat'l*

Graphics, Inc., 800 F.3d 1375, 1380 (Fed. Cir. 2015) (explaining that petitioners bear the initial burden to establish that the asserted references qualify as prior art)).

A petition must also identify, “in writing and with particularity, each claim challenged, the grounds on which the challenge to each claim is based, and the evidence that supports the grounds for the challenge to each claim[.]” 35 U.S.C. §312(a)(3); 37 CFR §42.104(b); *see Schlumberger Tech. Corp. v. Dynaenergetics Europe GmbH*, PGR2021-00089, Paper 13 at 40 (PTAB Dec. 14, 2021). Indeed, “[i]t is of the utmost importance that petitioners in IPR proceedings adhere to the requirement that the initial petition identify ‘with particularity’ the ‘evidence that supports the grounds for the challenge to each claim.’” *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016) (quoting 35 U.S.C. §312(a)(3)); *Schlumberger*, PGR2021-00089, Paper 13 at 40. The rules also require that each petition include “[a] full statement of the reasons for the relief requested, including a detailed description of the significance of the evidence including material facts, and the governing law, rules, and precedent.” 37 C.F.R. §42.22(a)(2).

“A reference patent or published patent application can be entitled to the benefit of its provisional application’s filing date for [§]102(e) purposes on two conditions. **First**, the provisional application must provide sufficient support for at least one claim in the reference patent or published patent application.... **Second**,

the provisional application must provide sufficient support for the **subject matter relied upon** for prior art purposes in the reference patent or published patent application.” *Google LLC v. Ikorongo Tech. LLC*, IPR2021-00058, Paper 14 at 10-11 (PTAB May 10, 2021) (citing, *inter alia*, MPEP §§2136(I) (9th ed. rev. 10.2019 June 2020), 2136.03(III), 2136); *see also Forescout Techs., Inc., v. Fortinet, Inc.*, IPR2021-01328, Paper 12 at 16-17 (PTAB Jan. 27, 2021).

Regarding the **second** requirement, Petitioner's burden is to prove the relied-upon subject matter was **also** fully disclosed in a ground reference's priority application. *See In re Giacomini*, 612 F.3d 1380, 1383 (Fed. Cir. 2010) (“[A]n applicant is not entitled to a patent if another's patent discloses the same invention, which was carried from an earlier U.S. provisional application or U.S. non-provisional application.”); *Forescout*, IPR2021-01328, Paper 12 at 8-10 (“[T]he subject matter in Thomas is **only** available as prior art to the '421 patent to the extent it **also** is described in the earlier-filed Thomas Provisional. Thus, **[Petitioner] has an initial burden**, not just to compare the challenged claims with the disclosure in Thomas, but **to show that the subject matter that [Petitioner] relies on in Thomas is also found in the Thomas Provisional.**”) (denying institution because Petitioner had not met its initial burden in the Petition); *see also Ex Parte Mann*, 2016 WL 7487271, at *5 (PTAB Dec. 21, 2016) (applying pre-AIA “subject matter test” to hold that “the provisional application must **also**

provide support for the subject matter relied upon in the rejection”) (emphasis in original).

Here, Petitioner fails to provide the necessary “full statement of the reasons for the relief requested, including a detailed explanation of the significance of the evidence,” particularly a detailed explanation of whether the Saxonov Provisional fully discloses the subject matter relied upon in the Petition—which is Petitioner’s burden to show that Saxonov qualifies as prior art. *See Schlumberger*, PGR2021-00089, Paper 13 at 41-49 (“Given the multiple instances in which Petitioner relies on subject matter in Sokolove ’009 without a detailed explanation of how either of the two earlier provisional applications support its position, we determine that Petitioner has not adequately identified the grounds and evidence that support the grounds with the required particularity.”); *Forescout*, IPR2021-01328, Paper 12 at 8-10.

Petitioner attempts to show the Saxonov Provisional supports Saxonov’s claim 1 (i.e., the first requirement described in, among other decisions, *Google* and *Forescout*). Petition, 11-15. However, Petitioner does **not** explain how either of the applications to which Saxonov nominally claims priority support the **disclosure** from Saxonov upon which Petitioner’s invalidity grounds rely (i.e., Petitioner does **not** satisfy the second requirement of, among other decisions, *Google*, *Forescout*, and *Giacomini*). *See* Petition, 30-46, 55-67. In

Telefonaktiebolaget, the Board explained: “Fatal to the Petition...[,] Petitioner did not establish that the subject matter relied upon for prior art was effectively filed in the provisional applications.... Petitioner does not assert, much less show, that the provisional applications satisfy the subject-matter requirement. Accordingly, Petitioner has not shown that [the asserted references] are entitled to priority dates of their provisional applications, and Petitioner has not shown a likelihood that it would prevail in its challenge to any claims of the [challenged] patent.”

Telefonaktiebolaget, IPR2022-00348, Paper 9 at 6.

This is exactly the case here, as will now be explained.

4. Petitioner Failed to Meet Its Burden of Showing Show the Relied-Upon Material Was Carried Over

When arguing Saxonov teaches the '051 Patent's claim limitations, Petitioner provides, at most, page:line citations to the Saxonov Provisional, summarized in the table below for Ground 1, claim 1. In no circumstance do these citations sufficiently (or even attempt to) explain the Saxonov Provisional's significance to Petitioner's grounds, nor establish that the Saxonov Provisional fully supports Petitioner's grounds.

Claim 1 limitation	Petitioner's Citation to Saxonov Provisional (EX1007)	Location in Petition of this citation to Saxonov Provisional
a) providing a sample solution volume	6:21-23, 6:13-15	30
comprising or potentially comprising, at least one of at least seven polynucleotide analytes	13:9-13, 15:12-22, 3:6-8, 17:4-10, FIG. 5, 5:19-6:3, 10:18-11:3	31-32
comprising at least seven hybridization probes, each hybridization probe corresponding to one of the at least seven polynucleotide analytes	13:14-17	34-35
wherein each hybridization probe comprises at least one fluorophore selected from four fluorophores	14:20-21, 4:20-23	36

Claim 1 limitation	Petitioner's Citation to Saxonov Provisional (EX1007)	Location in Petition of this citation to Saxonov Provisional
wherein each hybridization probe, when excited and when contacted with its corresponding polynucleotide analyte, generates a cumulative intensity signal	17:3-19:9, 18:5-21, 5:19-6:3	38-40
further wherein each generated cumulative intensity signal comprises at least one signal generated by excitement of at least one of the four fluorophores	17:4-19:9, 18:5-21, 5:19-6:3	40-41
b) contacting said sample solution volume with the plurality of hybridization probes	6:21-7:10, 12:21-13:8	41

Claim 1 limitation	Petitioner's Citation to Saxonov Provisional (EX1007)	Location in Petition of this citation to Saxonov Provisional
exciting the hybridization probes to generate the cumulative intensity signal(s) if one or more of the at least seven polynucleotide analytes is present in the sample volume	12:21-13:8	41-42
c) measuring the cumulative intensity signal(s), thereby generating a cumulative signal measurement	13:10-13, 17:4-19:23 (Example 3), 4:17-20, 5:19-6:5, 9:4-15, 10:8-11:3, 2:15-3:3, 12:31-13:8, FIG. 5, 5:19-6:5, 10:8-11:3, 9:4-15	42-43
wherein the cumulative signal measurement non-degenerately indicates the presence or absence of the at least seven polynucleotide analytes, in any combination of presence or absence	2:15-3:3, 3:15-4:20, 5:19-6:5, 9:4-10:3, 12:21-19:29, FIG. 5, 5:19-6:3	43

Claim 1 limitation	Petitioner's Citation to Saxonov Provisional (EX1007)	Location in Petition of this citation to Saxonov Provisional
wherein said method non-degenerately detects the presence or absence of the at least seven polynucleotide analytes in said single sample solution volume, in any combination of presence or absence	N/A	45
without requiring any step of immobilization of said polynucleotide analytes, physical separation of said polynucleotide analytes, or mass spectrometry	13:10-13, 17:4-19:23 (Example 3), 4:17-20, 5:19-6:5, 9:4-15, 2:15-3:3, 12:21-13:8, Examples 2-4, FIG. 5, 17:4-19:23 (Example 3), 4:17-20, 5:19-6:5, 9:4-15, 2:15-3:3, 12:21-13:8, Examples 2-4, FIG. 5)	46-47

Such bare citations to the Saxonov Provisional are insufficient, at least because the Petition “does not explain sufficiently the significance of the citations to the...provisional”—if any—and because “determining the significance of

the...citations would require [the Board] to play archeologist with the record,” which the Board should decline to do, as it has previously. *Google*, IPR2021-00058, Paper 14 at 13–15.

5. The Relied-Upon Subject Matter of Saxonov Was Not Carried Over from the Saxonov Provisional

Petitioner's failure to detail the significance (if any) of the Saxonov Provisional to the challenged claims is a symptom of a larger problem with the Petition: certain subject matter upon which Petitioner's grounds rely was **not** carried over from, or fully supported by, the Saxonov Provisional. Thus, for purposes of the grounds, Saxonov is not prior art any earlier than its **non-provisional** filing date of July 12, 2012, which was **after** the '051 Patent's earliest priority date (February 3, 2012).

For example, FIGS. 9 and 10 of Saxonov are absent from the Saxonov Provisional. EX2001, ¶45. Nor does any disclosure in the Saxonov Provisional, as understood by a POSA, support or disclose the subject matter relied on by Petitioner from these figures. *Id.* As another example, Saxonov's ¶¶17, 18, 37, 44, 69-71, and 76-80 contain significant new subject matter which is not found in, or supported by, the Saxonov Provisional. *Id.*, ¶46. The grounds rely upon this **newly added** subject matter for the challenged claims, for example as shown below in the table below for Ground 1, claim 1. *Id.*, ¶47.

Claim 1 limitation	Petitioner's Citation to subject matter in Saxonov (EX1004) not carried from Saxonov Provisional (EX1007)	Location in Petition of this citation to Saxonov
a) providing a sample solution volume	¶17	31-32
comprising at least seven hybridization probes, each hybridization probe corresponding to one of the at least seven polynucleotide analytes	FIG. 9, ¶77	34-35
wherein each hybridization probe comprises at least one fluorophore selected from four fluorophores	FIGS. 9, 10, ¶¶76-79	36
further wherein each generated cumulative intensity signal comprises at least one signal generated by excitement of at least one of the four fluorophores	FIG. 10, ¶¶37, 77, 79	40-41

Claim 1 limitation	Petitioner's Citation to subject matter in Saxonov (EX1004) not carried from Saxonov Provisional (EX1007)	Location in Petition of this citation to Saxonov
b) contacting said sample solution volume with the plurality of hybridization probes	FIG. 9, ¶¶ 17, 18, 77	41
exciting the hybridization probes to generate the cumulative intensity signal(s) if one or more of the at least seven polynucleotide analytes is present in the sample volume	FIG. 10 and ¶¶ 37 and 79	41-42
c) measuring the cumulative intensity signal(s), thereby generating a cumulative signal measurement	FIG. 10, ¶¶ 76-78	42-43
wherein the cumulative signal measurement non-degenerately indicates the presence or absence	FIGS. 9, 10, ¶¶ 17, 18, 76-79	43

Claim 1 limitation	Petitioner's Citation to subject matter in Saxonov (EX1004) not carried from Saxonov Provisional (EX1007)	Location in Petition of this citation to Saxonov
of the at least seven polynucleotide analytes, in any combination of presence or absence		
without requiring any step of immobilization of said polynucleotide analytes, physical separation of said polynucleotide analytes, or mass spectrometry	FIGS. 9, 10, ¶¶78-79	46-47

Saxonov's FIGS. 9 and 10 and ¶¶ 17, 18, 37, and 76-80 are **not** carried over from, and not fully supported by, the Saxonov Provisional. EX2001, ¶48. Therefore, Petitioner cannot establish that Saxonov is §102(e) prior art for purposes of its grounds. *Giacomini*, 612 F.3d at 1383; *Forescout*, IPR2021-01328, Paper 12 at 8–10; *Mann*, 2016 WL 7487271, at *5.

Saxonov also claims priority to U.S. App. No. 61/507,082, filed July 12, 2011. EX1004, §(60). However, Petitioner does not indicate (let alone sufficiently

explain) any reliance upon the subject matter or priority date of that application.

Instead, Petitioner cites only to the Saxonov Provisional.

Thus, Petitioner fails to establish that Saxonov qualifies as prior art. Because Petitioner relies on Saxonov for each ground, Petitioner has not demonstrated it is reasonably likely to prevail with respect to any claim or ground.

B. The Challenged Claims Are Patentable over the Ground References

Even assuming Saxonov could qualify as prior art (it cannot), the '051 Patent claims are patentable over Saxonov, whether alone or combined with the other ground references.

1. Ground 1, Claims 1-4: Saxonov

The Petition alleges claims 1-4 are obvious over Saxonov. Caltech disagrees, and the Board should as well.

a. Challenged claim 1 and Saxonov differ in kind, not just degree

While the '051 Patent and Saxonov both aim to extend the number of analytes that can be examined simultaneously, they solve these problems in significantly different ways. EX2001, ¶89.

For example, Saxonov tried to use the “same optical channel” to detect different analytes, ostensibly to reduce the cost of additional optical channels and optical dyes. EX2001, ¶90; *supra* §II.D.1. To detect different analytes, Saxonov

extensively diluted the sample into numerous droplets such that most of the droplets are empty (contain zero analyte molecules), and the next largest population of droplets contains a single analyte. *Id.*, ¶91; *supra* §II.D.1. Saxonov is replete with examples of how to identify a **single** analyte molecule within a droplet. *Id.*; *supra* §II.D.1. Indeed, for detecting multiple analytes in the same optical channel, droplets with a single analyte molecule are key to Saxonov's method. *Id.*, ¶92.

Because of the Poisson distribution, it is inevitable that some droplets will contain two analyte molecules, or even more than two (with frequency dropping quickly as the number of molecules/droplets increases). EX2001, ¶92. But such droplets are unnecessary in Saxonov's method for obtaining the desired results, because the single-molecule droplets unambiguously provide the desired data of whether individual analytes are present or absent in the sample. *Id.*

In comparison, the '051 Patent solves the problem of detecting different analytes in a sample by measuring cumulative optical signals using a coding scheme. EX2001, ¶94.

An important feature taught by the '051 Patent is how to choose probe colors and intensities that uniquely determine a given analyte, even if that analyte is mixed with other analytes at the same time. EX2001, ¶95. This avoids a degeneracy problem, where the same intensity values could be consistent for two

different analytes. *Id.* For example, if intensity values 1, 2, 4, 8, 16, 32 are chosen for probes read in the same optical channel, every combination of present/absent analytes is unique. *Id.* This method of decoding cumulative signals is different in kind (not just degree) from Saxonov, and makes it much easier to analyze multiplexed samples. *Id.*

Challenged claim 1 is directed to detecting the “presence or absence of **at least seven polynucleotide analytes**, in any combination of presence or absence, in a single sample solution volume.” The sample solution volume also includes “**at least seven hybridization probes**, each...corresponding to one of the at least seven polynucleotide analytes” and comprising “at least one fluorophore selected from four fluorophores.” Claim 1 recites generating a cumulative intensity measurement that “**non-degenerately** indicates the presence or absence of the at least seven polynucleotide analytes, **in any combination of presence or absence**.” The claimed method provides flexibility to detect any possible combination of the analytes within the single sample solution volume, in such a manner that each analyte may be uniquely distinguished from each other analyte. *Supra* §II.B. At the time of the '051 Patent and its priority applications, this was a new, non-obvious, and useful solution to the problem of how to increase the number of analytes that could be non-degenerately detected. *Supra* §II.B.; EX2001, ¶43.

b. **Saxonov does not teach how to identify three or more analyte molecules within a droplet**

Droplets containing more than one analyte were unnecessary in Saxonov's method for obtaining the desired results, because the single-molecule droplets unambiguously provided the desired information about whether individual analytes are present or absent in the sample. EX2001, ¶97. To the extent that Saxonov contemplates identifying three or more analytes a given droplet, Saxonov falls far short of describing how to actually do so. *Id.*, ¶98. This is because Saxonov had no need to try to solve that problem, the single-analyte droplets yielding the information that Saxonov apparently sought—an identification of whether an analyte was present in the sample. *Id.* Saxonov did not contemplate the solution provided by the '051 Patent, because there was no need in Saxonov to even contemplate the possibility of a large number of analytes per droplet—Saxonov's limiting dilution avoided this issue—let alone solve the problem of how to non-degenerately identify that many analytes. *Id.*

Saxonov fails to teach how to non-degenerately distinguish even **three** analytes in a droplet, let alone more (like the recited “at least seven”). EX2001, ¶99. Illustratively, Saxonov provides the following table purporting to describe the “Intensity” of each of eight ($2^{N=3}$) clusters for three analytes in a single channel:

	Target A	Target B	Target C	Intensity
Population 8	+	+	+	Highest
Population 7	+	+	–	Intermediate
Population 6	+	–	+	Intermediate
Population 5	–	+	+	Intermediate
Population 4	+	–	–	Intermediate
Population 3	–	+	–	Intermediate
Population 2	–	–	+	Intermediate
Population 1	–	–	–	Lowest

EX1004, ¶41. However, Saxonov does not explain the differences (if any) amongst the various “Intermediate” intensities, nor whether such intensities are non-degenerate, nor how such differences (if any) might be detected using just a single channel. EX2001, ¶100. Indeed, Saxonov merely “*assume*[s] that each population is distinguishable.” EX1004, ¶41; EX2001, ¶100.

As another example, Saxonov’s FIG. 10 and ¶¶77-79 (which were not carried over from the Saxonov Provisional but are cited in Petitioner’s grounds (*see supra* §V.A.5.)), further highlight Saxonov’s failure to teach how to obtain meaningful information from droplets containing three or more analytes (let alone at least seven analytes, as recited in ’051 Patent claim 1). EX2001, ¶101. Saxonov states that double-positive populations (T1+/T2+, T1+/T3+, and T2+/T3+) and the triple-positive population (T1+/T2+/T3+) in FIG. 10 are not shown “[t]o simplify the presentation” but “may be resolved and distinguishable from one another and

from the single-target populations and the negative population.” EX1004, ¶¶78-79; EX2001, ¶101. But Saxonov does not actually explain **how** populations of droplets that contain three or more analytes (let alone at least **seven** analytes) might actually be “resolved and distinguishable from one another”—let alone in the specific manner recited in claim 1. EX1004, ¶¶78-79; EX2001, ¶101.

c. **Petitioner's proposed probe schemes based on Saxonov contradict Saxonov's own teachings and omit that which is recited in claim 1**

Despite Saxonov's significant shortcomings, Petitioner tries to use Saxonov's teachings (many of which are not even prior art, *supra* §V.A.) as a jumping-off point to propose two different probe schemes for detecting eight or nine analytes, which allegedly render obvious claim 1 (which recites non-degenerately distinguishing among at least “seven” analytes). Petition, 32-34. Sections V.B.1.c.(1)-(3) below discuss Petitioner's schemes—which do not actually appear in Saxonov—to help explain the shortcomings. EX2001, ¶102.

(1) **Summary of Petitioner's proposed probe schemes**

Petitioner's first proposed scheme, shown below, is for three colors and three intensities per color, which according to Petitioner “would allow the non-degenerate identification of **nine** different analytes.” Petition, 33 (emphasis in original); EX1002, ¶157.

	Color 1	Color 2	Color 3
Intensity 1	Analyte 1	Analyte 4	Analyte 7
Intensity 2	Analyte 2	Analyte 5	Analyte 8
Intensity 3	Analyte 3	Analyte 6	Analyte 9

In the second proposed scheme, reproduced below, Petitioner asserts that using four colors and two intensities per color, “***eight*** analytes can be unambiguously detected.” Petition, 34 (emphasis original); EX1002, ¶159.

	Color 1	Color 2	Color 3	Color 4
Intensity 1	Analyte 1	Analyte 3	Analyte 5	Analyte 7
Intensity 2	Analyte 2	Analyte 4	Analyte 6	Analyte 8

Petitioner asserts that “both schemes described—three colors at three intensities and four colors at two intensities—allow for the analysis of samples that have at least seven analytes and a POSA would have reasonably expected success in using either scheme contemplated in Saxonov.” Petition, 34; EX1002, ¶160. Petitioner concludes that Saxonov teaches “assays that are non-degenerate by

design in the same manner, and for the same reasons, as the analogous assays using single color labels of varying intensity disclosed in the '051 patent.” Petition, 44 (citing EX1002, ¶¶205-206; EX1001, 25:1-2, 23:41-43, 23:59-24:19 (Table 8)). Notably, Petitioner primarily cites the **'051 Patent—not Saxonov**—to show how Saxonov's purported schemes supposedly work in the “same manner” and “for the same reasons” as those of the challenged claims. EX2001, ¶106.

(2) **Petitioner's proposed probe schemes contradict Saxonov's own teachings**

Petitioner's schemes so vastly oversimplify and mischaracterize Saxonov's disclosure that they contradict Saxonov's own teachings. EX2001, ¶107. More specifically, Petitioner's proposed eight- and nine-analyte schemes include intensities and colors only for **single-analyte** droplets; this is clearly reflected in each of their boxes containing only **one** analyte (e.g., “Analyte 1,” “Analyte 2,” etc.). Petition, 33-34; EX2001, ¶107. Petitioner's schemes do **not** represent any droplets containing **two** analytes (e.g., do not include boxes containing Analyte1+Analyte2 or Analyte3+Analyte8), nor containing **three** analytes (e.g., do not include a box containing Analyte 4+Analyte6+Analyte8), let alone containing **more than three** analytes. Petition, 33-34; EX2001, ¶107.

This is contrary to Saxonov's express teaching that “data including all permutations of positives will generally fall into 2^N populations or clusters, where

N is the number of targets, assuming that each population is distinguishable.”

EX1004, ¶41; EX2001, ¶108. Furthermore, a POSA would have understood that there would be N number of single analyte droplets and (2N minus N) number of multi-analyte droplets. EX2001, ¶108. From this teaching, a POSA would have understood Saxonov to teach N=8 analytes yields 256 clusters ($2^8=256$), eight for single-analyte droplets and **248** (256 minus 8) for multi-analyte droplets. EX1004, ¶41; EX2001, ¶107. Additionally, a POSA would have understood Saxonov to teach N=9 analytes yields 512 clusters ($2^9=512$), nine for single-analyte droplets and **503** (512 minus 9) for multi-analyte droplets. EX1004, ¶41; EX2001, ¶107.

Petitioner does not attempt to represent even a subset (let alone all) of the **248** multi-analyte droplets in the eight-analyte scheme; nor even a subset (let alone all) of the **503** multi-analyte droplets in the nine-analyte scheme. EX2001, ¶109. As such, Petitioner's oversimplified representations ignore Saxonov's express teachings about the number of clusters their purported schemes would actually produce. *Id.* If Petitioner were to argue that they omitted the multi-analyte droplets from their representations for simplicity, this would merely mirror Saxonov's own deficiencies regarding multi-analyte droplets. *Id.*; *supra* §§II.D.1, V.B.1.c.(1).

(3) **Petitioner's proposed probe schemes omit that which is allegedly obvious**

Petitioner's schemes further are so vastly oversimplified that they omit that which Saxonov allegedly renders obvious. EX2001, ¶110. Claim 1 recites the cumulative measurement signal “non-degenerately indicates the presence or absence of the at least seven polynucleotide analytes, *in any combination of presence or absence.*” As noted above in §V.B.1.c.(1), Petitioner's proposed eight- and nine-analyte schemes include intensities and colors only for *single-analyte* droplets, omitting any droplets containing *two, three, or more than three* analytes, and certainly not representing “*any* combination of presence or absence” of at least *seven* polynucleotide analytes. Petition, 33-34; EX2001, ¶110. Petitioner's failure even to represent this key claim feature in their purported eight- and nine-analyte schemes speaks volumes about how far their strained interpretation of Saxonov falls short of teaching all that is recited in claim 1. EX2001, ¶109.

d. **Petitioner inappropriately disregards recitations of claim 1**

The Board should also decline Petitioner's invitation to ignore numerous clauses of the '051 Patent claims. One such clause is “wherein said method non-degenerately detects the presence or absence of the at least seven polynucleotide analytes in said single sample solution volume, in any combination of presence or absence.” Petition, 45. Petitioner argues that because this clause “merely states

the desired outcome of the claim and is redundant of prior claim elements, it is not entitled to any patentable weight.” Petition, 45 (citing EX1002, ¶208). Petitioner is wrong for multiple reasons.

First, after extensively examining the claims—including specifically considering Saxonov (and Kramer) in IDSs—the Examiner allowed the application, stating “[t]he claims recite a new and non-obvious assay to detect the presence/absence pattern of seven different analytes using non-degenerate hybridization techniques.” EX2003, 2658; *supra* §II.C. The Examiner’s careful analysis and allowance over Saxonov (and Kramer) provides significant evidence of patentability over Saxonov (and Kramer) that Petitioner cannot simply disregard.

Second, Petitioner’s only support for reading out this clause comes from Dr. Batt. Petition, 45 (citing EX1002, ¶208). But Dr. Batt is a technical expert, not a patent attorney; he is not qualified to opine on the legal issues of whether claim language is entitled to any patentable weight.

Third, Petitioner’s position is illogical. If the clause is redundant as Petitioner suggests, keeping the clause would simply reaffirm what is recited elsewhere in the claim. So it would be improper to ignore this language.

Petitioner similarly oversimplifies PO’s infringement contentions in the parallel litigation in an attempt to avoid addressing the actual claim language. For

example, Petitioner argues “[a]s Dr. Batt explains, the assays in Saxonov using droplets are the exact same types of assays detecting the presence of polynucleotide analytes in droplets that [PO] accuses of infringing in parallel litigation.” Petition, 45 (citing EX1002 ¶¶ 209-210; Petition, §X.A.13).

But Dr. Batt’s analysis is conclusory and lacks support; he does not specifically explain *why* the assays in Saxonov should be construed to be “the exact same types of assays” that are accused of infringement in parallel litigation. See EX1002, ¶¶209-210. Instead, Dr. Batt merely states that “[b]oth employ the use of dPCR involving droplets and are directed to determining the presence or absence of analytes in each droplet” *Id.*, ¶210 (citing EX1012). Dr. Batt states his “opinion [that] the assays in Saxonov are wholly consistent with those identified in [PO’s] infringement contentions, which contend that the determination of polynucleotide analytes in droplets are infringing.” *Id.*, ¶210 (citing EX1012). But PO does not merely contend in the parallel litigation that Petitioner’s multiplexing technology that “unambiguously identify multiple targets using the same color tag” infringes the ’051 Patent. See, e.g., EX1028, 3. Instead, PO establishes how the accused devices perform each and every claimed method step of the claimed method. See EX1012. Accordingly, Dr. Batt’s reductionist “opinion” is incorrect and should be disregarded.

For at least these reasons, the Board should reject Petitioner's attempts to (1) revise Saxonov to cast it as teaching more than it does; (2) revise the prosecution history of the '051 Patent to cast the claims as reciting fewer limitations than they do; and (3) revise the infringement contentions in the parallel litigation to cast the claims as encompassing the prior art. Instead, the Board should find Petitioner has failed to show that it has a reasonable likelihood of prevailing on Ground 1.

2. Ground 2, Claims 5-6: Saxonov and Silverbrook

Petitioner alleges claims 5-6 are obvious over Saxonov in view of Silverbrook. Petition, 49-51. Claims 5-6 depend from and add limitations to claim 1. Petitioner does not assert Silverbrook teaches the features of claim 1 discussed above that Saxonov fails to disclose. Rather, Petitioner uses Silverbrook's teachings relating to "transmit[ing] information through a computer network" (claim 5) and "provid[ing] information concerning the presence or absence of polynucleotide analytes to a healthcare professional" (claim 6). *Id.*, 50, 51. At least because Silverbrook does not cure Saxonov's failure regarding claim 1, the Petition also fails regarding claims 5-6.

3. Ground 3, Claim 7: Saxonov and Maltezos

Petitioner alleges claim 7 is obvious over Saxonov in view of Maltezos. Petition, 51-52. Petitioner does not assert Maltezos teaches the features of claim 1 discussed above that Saxonov fails to disclose. Rather, Petitioner uses Maltezos's

teachings relating to a “computer [allegedly] perform[ing] the detecting and/or measuring step.” *Id.* At least because Maltezos does not cure Saxonov's failure regarding claim 1, the Petition also fails regarding claim 7.

4. Ground 4, Claims 8-9: Saxonov, Maltezos, and Oh

Petitioner alleges claims 8-9 are obvious over Saxonov in view of Maltezos and Oh. Petition, 52-53. Petitioner cites Maltezos for claim 7, addressed in §V.B.3. above. Regarding claim 8, Petitioner argues “[g]iven the teachings of Saxonov and Oh, a POSA would have found it obvious to use a remote computer to perform the measuring (and calculating) step.” *Id.*, 53. Regarding claim 9, Petitioner argues a POSA would have been motivated to locate Oh's “computing unit 41” “on the thermal cyclor for the benefits discussed above and would have had a reasonable expectation of success.” *Id.*, 54-55. But at least because Petitioner does not explain how Oh cures Saxonov's deficiencies for claim 1, the Petition also fails regarding claims 8-9.

5. Ground 5, Claims 1-4: Saxonov, Kramer, and/or Larson

For Ground 5, Petitioner alleges claims 1-4 are obvious over Saxonov in view of Kramer and/or Larson. Petition, 55 et seq. Ground 5 fails for multiple reasons.

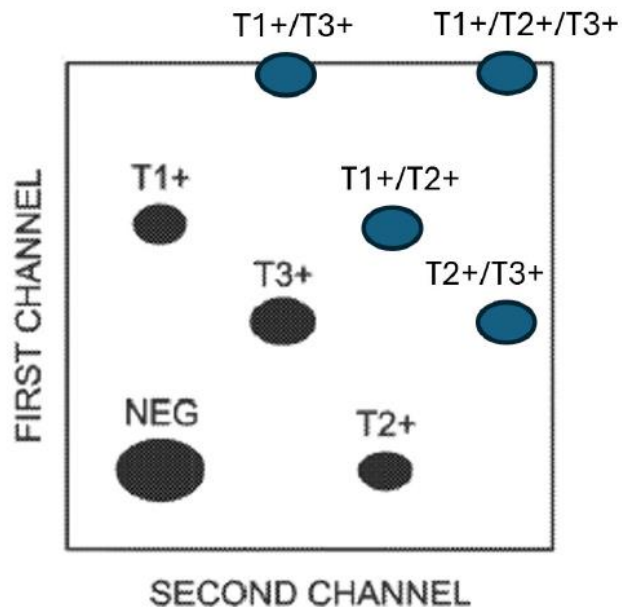
a. **Saxonov is equally deficient for this ground**

Petitioner relies heavily on Saxonov's FIG. 10 and ¶¶18, 78, and 79 (*see, e.g.,* Petition, 56-57, 62-64). However, these portions of Saxonov are not carried over from the Saxonov Provisional, and not entitled to priority for purposes of this Ground 5 for the same reasons described *supra* §V.A.

Moreover, Saxonov's teachings (which are not entitled to priority) fall far short of rendering claim 1 obvious for the same reasons discussed above for Ground 1. *Supra* §V.B.1. Indeed, in Ground 5, Petitioner finds even more creative ways to stretch and revise Saxonov. EX2001, ¶115. The Board should similarly disregard these fabrications.

Illustratively, Petitioner proffers the following fabricated version of Saxonov's FIG. 10, which includes the double-positive and triple-positive clusters that Saxonov did not actually illustrate.

Fig. 10

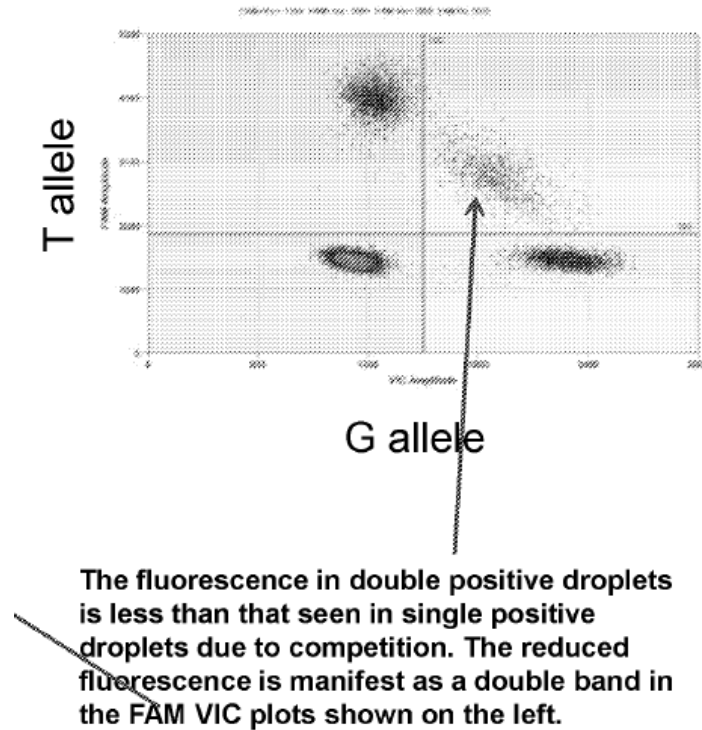


Petition, 65; EX2001, ¶116.

Here, Petitioner adds double-positive clusters T1+/T3+, T1+/T2+, T2+/T3+, and triple-positive cluster T1+/T2+/T3+, and states that “[a]s this modified figure shows, any combination of three targets may be uniquely identified.” Petition, 65; EX2001, ¶117. However, Petitioner does not explain its basis (if it had any) for alleging the particular cluster locations added to FIG. 10. EX2001, ¶117. Instead, Petitioner’s expert merely concludes without supporting evidence or analysis that “[a]s shown, droplets with any combinations of the three targets can be identified.” EX1002, ¶302.

The Board should not accept Petitioner’s fabricated representation, for example because the Saxonov Provisional actually shows a double-positive result

in a different location than Petitioner asserts. More specifically, the Saxonov Provisional shows a plot of two analytes (here, the T and G alleles) in two channels, plus an arrow and annotation:



EX1007, 58.

A POSA would have understood the lower right cluster to be “single positive” for the G allele and the upper left cluster to be “single positive” for the T allele. EX2001, ¶119. The Saxonov Provisional refers to the middle cluster (where the arrow points), as “[t]he fluorescence in **double positive** droplets.”

EX1007, 58. A POSA would readily have understood that this double-positive cluster does **not** occur at a location corresponding to the neat and simple sum of the single positive clusters (as Petitioner’s modified FIG. 10 represents), but instead is

shifted to another location because of reduced fluorescence “***due to competition.***” EX1007, 58; EX2001, ¶120. Accordingly, a POSA would have expected double-positive and the triple-positive clusters (if any) to occur in ***different locations*** than Petitioner's modified FIG. 10 asserts. *Id.*, ¶120. Accordingly, this modified figure (and Petitioner's discussion thereof) should be disregarded as fiction.

For at least these reasons, Petitioner has failed to show it has a reasonable likelihood of prevailing on Ground 5.

b. Kramer and Larson do not cure Saxonov's deficiencies

Petitioner attempts to use Kramer and Larson to cure Saxonov's deficiencies, but fails here too.

(1) Kramer

Petitioner falls short of explaining why a POSA would have found it obvious to try to combine Kramer with Saxonov to detect at least seven polynucleotide analytes, ***in any combination of presence or absence***, in a single sample solution volume. EX2001, ¶122. More specifically, Petitioner proffers the following rationale for combining Saxonov with Kramer:

It would have been obvious to modify the two-color approach in Figure 10 of Saxonov, which is used for three targets, for the detection of at least seven targets. EX1002 ¶292. One would have done this by ***increasing***

*the number of colors and then using intensity as needed
to distinguish droplet types*, as taught in Kramer[.]²

Petition, 60; EX2001, ¶122.

However, Kramer actually states that “preferred assays that are **not** highly likely to find only one target utilize **strictly** combinational coding.” EX1008, ¶32; EX2001, ¶123. Accordingly, Kramer would not have motivated a POSA attempting to perform assays intended to accommodate **multiple** analytes per sample solution volume (as in claim 1) to attempt to use “intensity as needed to distinguish droplet types,” as Petitioner proposes. EX2001, ¶124. Accordingly, Petitioner’s proffered rationale fails, and Petitioner has not shown a reasonable likelihood of prevailing on Ground 5.

(2) **Larson**

Petitioner also falls short of explaining why a POSA would have found it obvious to try to combine Larson with Saxonov to detect at least seven polynucleotide analytes, **in any combination of presence or absence**, in a single sample solution volume. EX2001, ¶128. Here, Petitioner alleges Larson teaches that “differences in intensity can be used to distinguish droplets with different

² Saxonov’s FIG. 10, cited here too, was not carried from and is not supported by the Saxonov Provisional. *Supra* §V.A.5.

target types, showing data for an assay that distinguishes droplets [with] nine different types of targets:”

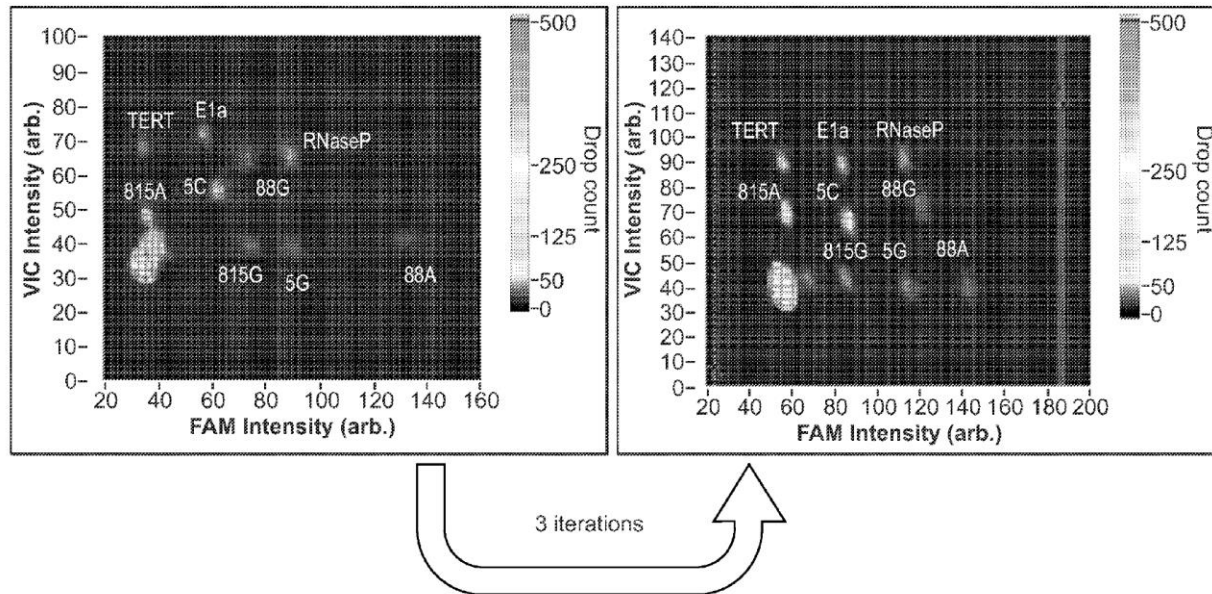


FIG. 15

Petition, 59 (citing EX1017, FIG. 15, ¶¶34, 145-153).

But like Saxonov's FIG. 10, Larson's FIG. 15 includes only *single-analyte* clusters (e.g., TERT, 815A, E1a, 5C, 815G, RNaseP, 88G, 5G, 88A). EX1017, FIG. 15; EX2001, ¶126. The absence in Larson's FIG. 15 of any double-, triple-, or even higher-multiple-positive clusters indicates that the droplets Larson measured contained a *single* analyte, and this is consistent with Larson's repeated teachings to use a single analyte per droplet. *Supra* §II.D.3. A POSA would not have found Larson's teachings at all instructive on how to detect at least seven

polynucleotide analytes, ***in any combination of presence or absence***, in a single sample solution volume. EX2001, ¶127.

For at least this additional reason, Petitioner has not shown a reasonable likelihood of prevailing on Ground 5.

6. Grounds 6-8, Claims 5-9

Petitioner alleges claims 5-9 are obvious over Saxonov combined with Kramer and/or Larson further in view of Silverbrook (claims 5-6), Maltezos (claim 7), and Maltezos and Oh (claims 8-9),³ “for the same reasons in Grounds 2-4.” Petition, 67. Sections V.B.1-5. establish that claims 5-9 are not obvious over Saxonov in view of these references. Even assuming Silverbrook, Maltezos, and Oh teach what Petitioner alleges (they do not), Petitioner has not explained how they cure the many deficiencies of Saxonov, Larson, and Kramer detailed above. *See supra* §§V.B.1-5. Thus, Petitioner has failed to show it has a reasonable likelihood of prevailing on grounds 6-8.

C. The Board Should Deny Under §314(a) and *Fintiv*

Overall, the *Fintiv* factors weigh in favor of discretionary denial.

³ Petitioner's arguments at Petition, 67 do not clearly identify what Ground 8 consists of, are inconsistent with Petitioner's table at Petition, 26-27, and primarily refer to claims 6-9 rather than claims 5-9.

1. Factor 1: Likelihood of a Stay

This factor is neutral. While Petitioner asserts “[t]his factor weighs in favor of institution because Petitioner will seek a stay if IPR is instituted and stays are favored in the Northern District of California” where the parallel action is pending (Petition at 70), the Board should “decline to speculate on how the district court might rule on a motion that has not been filed...[and] assess this factor as neutral” (*Carrier Fire & Security Ams. Corp. v. Sentrilock, LLC*, IPR2021-00665, Paper 12 at 8 (PTAB Sept. 16, 2021)). *See also Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 15 at 12 (PTAB May 13, 2020) (“A judge determines whether to grant a stay based on the facts of each specific case as presented in the briefs by the parties. We decline to infer, based on actions taken in different cases with different facts, how the District Court would rule should a stay be requested by the parties in the parallel case here. This factor does not weigh for or against discretionary denial in this case.”); *Sotera Wireless, Inc. v. Masimo Corp.*, IPR2020-01019, Paper 12 at 14 (PTAB Dec. 1, 2020) (“Because the District Court has not ruled on the pending motion to stay, we determine that this factor does not weigh for or against denying institution in this case.”); *Zomm, LLC v. Apple Inc.*, 391 F. Supp. 3d 946, 956 (N.D. Cal. 2019) (“Courts...must evaluate stay requests on a case-by-case basis.”); *see also Precision Planting LLC v. Maschio Gaspardo S.p.A.*, IPR2024-00008, Paper 12 at 16 (PTAB Mar. 26, 2024).

2. Factor 2: Proximity of Trial Date to a Final Written Decision

This factor weighs in favor of denial. Under PO's proposed schedule in the parallel litigation, trial will commence in the first half of January, 2026 even assuming the district court does not issue a *Markman* order until two months after the hearing, which is scheduled for December 12, 2024. See EX2014, 18-20; EX2013. Thus, under PO's schedule the Board's deadline to issue a final decision—January 31, 2026—is after trial in the parallel litigation will commence. This favors discretionary denial. *Fintiv*, IPR2020-00019, Paper 15 at 13 (factor 2 weighed in favor of denial where trial was scheduled to begin before FWD deadline).

3. Factor 3: Investment in the Parallel Litigation

This factor weighs in favor of denial.

In *Fintiv*, the Board found this factor weighed somewhat in favor of denial in circumstances similar to those here. See *Fintiv*, IPR2020-00019, Paper 15 at 13–14. Particularly, *Markman* had been fully briefed, contentions were served, fact discovery was in early stages, document production was ongoing, depositions were in early stages, expert reports were not due yet, and substantive motion practice was yet to come. *Id.* Thus, “the parties and the Court [had] invested effort in the District Court case..., [and while] further effort remain[ed] to be expended

in this case before trial[,] [b]ased on the level of investment and effort already expended on claim construction and invalidity contentions in the District Court, this factor weighs somewhat in favor of discretionary denial in this case.” *Id.*; see also *Sand Revolution II, LLC v. Cont’l Intermodal Group – Trucking LLC*, IPR2019-01393, Paper 24 at 10–11 (PTAB June 16, 2020) (similar).

Here—as of the time of this filing—similar to *Fintiv* and *Sand Revolution*, ChromaCode and Caltech have served infringement contentions, Petitioner and Caltech have exchanged damages contentions, Petitioner has served invalidity contentions, the court has entered an ESI order, *Markman* briefing is complete, and fact discovery is ongoing. Thus, while additional work remains, the parties and the court have invested in the case, including but not limited to invalidity and claim construction.

This case will progress even further between now and when the Board decides institution, which is the proper time to assess this factor. See *T-Mobile USA, Inc. v. Wireless Alliance, LLC*, No. IPR2024-00607, Paper 16 at 11 (PTAB Sept. 10, 2024) (“We consider now the amount and type of work that will have already been completed in the parallel litigation by the court and the parties at the time of our institution decision.”). Particularly, a tech tutorial and *Markman* hearing are scheduled for the first half of December, and the parties are well into fact discovery, which PO expects will close on within a few months of the court’s

Markman order issuing. *Supra* §II.E. PO expects exchange of opening and rebuttal expert reports will be completed shortly thereafter. *See id.* The institution decision here is expected in January 2025. “Because the *Markman* hearing will be completed prior to the time of the institution decision and discovery will have proceeded to an advanced stage...by the time of this Decision, [the Board should] find that factor 3 weighs in favor of exercising discretion to deny institution.” *T-Mobile USA, Inc. v. Cobblestone Wireless, LLC*, No. IPR2024-00136, Paper 18 at 16–17 (PTAB June 5, 2024).

4. Factor 4: Overlap of Issues

In the parallel litigation—just as in the Petition—Petitioner contends claims 1–9 of the ’051 Patent are invalid based upon combinations of Saxonov,⁴ Larson, and Kramer—one or more of which form a basis for each and every petitioned ground. *Compare, e.g.*, EX2008 and EX2009 with Petition at 26–27. “[B]ecause the identical claims are challenged based on the same prior art in both the Petition

⁴ In its invalidity contentions, Petitioner asserts Saxonov is prior art under §102(g) (*see, e.g.*, EX2006, 4), but in the claim charts appended to the contentions, Petitioner relies on the published Saxonov application relied on in the grounds here (*compare, e.g.*, EX2008 with Petition, 11).

and in the District Court, this factor weighs in favor of discretionary denial in this case.” *Fintiv*, IPR2020-00019, Paper 15 at 15.

While Petitioner asserts this factor is neutral given the “extensive additional art and issues” being litigated in the district court, Petitioner does not cite any authority to support this position. Regardless of whether the ground references are a subset of the art Petitioner asserts in the parallel litigation, the reality is that there is overlap. Moreover, Petitioner has not filed a *Sotera* stipulation. Thus, “as no *Sotera* stipulation has been filed and the same art and overlapping claims are at issue in the related cases, this factor weighs in favor of denial.” *Commscope Techs. LLC v. Dali Wireless, Inc.*, IPR2022-01293, Paper 18 at 15 (PTAB March 9, 2023).

5. Factor 5: Whether Petitioner Is the Defendant in the Parallel Litigation

Here, Bio-Rad is both Petitioner here and defendant in the parallel litigation. “Because the petitioner and the defendant in the parallel proceeding are the same party, this factor weighs in favor of discretionary denial.” *Fintiv*, IPR2020-00019, Paper 15 at 15; *see also Sotera Wireless, Inc. v. Masimo Corp.*, IPR2020-01019, Paper 12 at 19 (PTAB Dec. 1, 2020) (“Petitioner and Patent Owner acknowledge the parties are the same in the *inter partes* proceeding and in the parallel proceeding. Thus, this factor supports denying institution.”); *Commscope Techs.*

LLC v. Dali Wireless, Inc., IPR2022-01293, Paper 18 at 15–16 (PTAB March 9, 2023) (“Petitioner is the defendant in several of the parallel proceedings. Petitioner does not dispute this. This factor weighs in favor of exercising our discretion to deny the Petition.”) (citations omitted); *T-Mobile*, IPR2024-00607, Paper 16 at 15 (“[W]e determine, applying Board precedent, that this factor weighs in favor of a discretionary denial” “where the parties in the parallel litigation are the same as in the *inter partes* proceeding.”) (internal quotation marks and citations omitted). Bio-Rad asserts that because this is common, this factor is neutral, but cites no supporting authority. Petition, 73.

6. Factor 6: Other Circumstances, Including the Merits

This factor favors denial at least because Petitioner has not demonstrated it is “highly likely” to prevail with respect to at least one challenged claim. “[A] full analysis of the merits is not necessary to evaluate this factor. It is sufficient that Patent Owner has pointed out that Petitioner’s case...is a close call.... [If so,] [t]he merits, taken as a whole, do not tip the balance in favor of Petitioner and instead also weigh in favor discretionary denial in a balanced assessment of all the circumstances.” *Fintiv*, IPR2020-00019, Paper 15 at 17.

“As [Director Vidal’s] Guidance Memo and [the Board’s] precedential decision in *OpenSky* make clear, the compelling merits standard is a **higher standard** than the standard for institution set by statute.” *Commscope*, IPR2022-

01242, Paper 23 at 3; *OpenSky Indus., LLC v. VLSI Tech. LLC*, IPR2021-01064, Paper 102 at 49 (PTAB Oct. 4, 2022) (precedential). “A challenge can only ‘plainly lead to a conclusion that one or more claims are unpatentable’ if it is **highly likely** that the petitioner would prevail with respect to at least one challenged claim.” *Commscope*, IPR2022-01242, Paper 23 at 3–4 (quoting *OpenSky*, IPR2021-01064, Paper 102 at 49). “The patent system and the public benefit from instituting challenges where there is a showing of unpatentability by compelling merits, but it is **only** a finding under this **higher standard** that would compel the Board to review claims for the public benefit when other considerations favor discretionary denial.” *Commscope*, IPR2022-01242, Paper 23 at 4.

In view of the above, each of the *Fintiv* factors is either neutral or weighs against institution. Thus, even if the Board finds that Petitioner has demonstrated a reasonable likelihood of successfully invalidating one of the '051 Patent's claims (Petitioner has failed to do so for the reasons discussed in §V.B.), the Board should nevertheless exercise its discretion in view of *Fintiv* and deny institution.

VI. CONCLUSION

For at least these reasons, the Board should deny institution.

Respectfully submitted,

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Date: October 31, 2024

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I hereby certify that on October 31, 2024, a copy of the foregoing PATENT OWNER'S PRELIMINARY RESPONSE was filed through the Patent Trial and Appeal Case Tracking System (P-TACTS) and was served via Federal Express and E-Mail on the Petitioner at the following correspondence address provided by counsel of record for the Petitioner pursuant to 37 C.F.R. § 42.8(b)(4):

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**CERTIFICATE OF COMPLIANCE WITH
TYPE-VOLUME LIMITATION, TYPEFACE REQUIREMENTS,
AND TYPE STYLE REQUIREMENTS**

1. This Petition complies with the type-volume limitation of 14,000 words, comprising 12,782 words, as counted using the Microsoft Word software that was used to prepare this paper, excluding the parts exempted by 37 C.F.R. § 42.24(a).

2. This Petition complies with the general format requirements of 37 C.F.R. § 42.6(a) and has been prepared using Microsoft® Word in 14-point Times New Roman.

Respectfully submitted,

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