IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,	:	
Plaintiff,	:	
v.	:	C.A. No. 17-275-LPS-CJB
	:	C.A. No. 17-1353-LPS-CJB
OXFORD NANOPORE TECHNOLOGIES, INC. and OXFORD NANOPORE TECHNOLOGIES, LTD.,	:	
Defendants.	:	

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MEMORANDUM OPINION

March 6, 2019
Wilmington, Delaware

STARK, U.S. District Judge:

Plaintiff Pacific Biosciences of California, Inc. ("PacBio" or "Plaintiff") has brought two patent infringement suits against Defendants Oxford Nanopore Technologies, Inc. ("Oxford" or "Defendant") and Oxford Nanopore Technologies, Ltd. ("ONT LTD") asserting U.S. Patent Nos. 9,546,400 (the "'400 patent"), 9,772,323 (the "'323 patent"), 9,678,056 (the "'056 patent"), and 9,738,929 (the "'929 patent"). The four patents-in-suit generally relate to nanopore sequencing.

Presently before the Court is the issue of claim construction. PacBio and Oxford[1] submitted two technology tutorials (*see* D.I. 98, 99), objections to one of the technology tutorials (*see* D.I. 126), claim construction briefs (*see* D.I. 91, 92, 124, 127), exhibits (*see* D.I. 80, 91, 94, 125, 128), and expert declarations (*see* D.I. 95, 96, 97).[2] The Court held a claim construction hearing on December 17, 2018, at which both sides presented oral argument. (*See* D.I. 135 ("Tr."))

I. LEGAL STANDARDS

The ultimate question of the proper construction of a patent is a question of law. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (citing *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388-91 (1996)). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (internal quotation marks omitted).

"[T]here is no magic formula or catechism for conducting claim construction." *Id.* at

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[1] ONT LTD did not participate in claim construction.

[2] Unless otherwise specified, docket citations are to C.A. No. 17-275, but apply equally to C.A. No. 17-1353.

1324. Instead, the Court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.*

"[T]he words of a claim are generally given their ordinary and customary meaning . . . [which is] the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id.* at 1312-13 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). The patent specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

While "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding words of the claim also must be considered. *Phillips*, 415 F.3d at 1314. Furthermore, "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment . . . [b]ecause claim terms are normally used consistently throughout the patent." *Id.* (internal citation omitted).

It is likewise true that "[d]ifferences among claims can also be a useful guide. . . . For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15 (internal citation omitted). This "presumption is especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim, and one party is urging that the limitation in the dependent claim should be read into the independent claim." *SunRace Roots Enter. Co., Ltd. v. SRAM Corp.*, 336 F.3d 1298, 1303 (Fed. Cir. 2003).

It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. It bears emphasis that "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)) (internal quotation marks omitted).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). The prosecution history, which is "intrinsic evidence," "consists of the complete record of the proceedings before the PTO [Patent and Trademark Office] and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*

In some cases, "the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d

at 980. For instance, technical dictionaries can assist the court in determining the meaning of a term to those of skill in the relevant art because such dictionaries "endeavor to collect the accepted meanings of terms used in various fields of science and technology." *Phillips*, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* Furthermore, "statements made by a patent owner during an IPR [inter partes review] proceeding . . . can be considered for claim construction." *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353, 1362 (Fed. Cir. 2017). Overall, while extrinsic evidence "may be useful" to the court, it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

Finally, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). It follows that "a claim interpretation that would exclude the inventor's device is rarely the correct interpretation." *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1358 (Fed. Cir. 2007)

(quoting *Modine Mfg. Co. v. U.S. Int'l Trade Comm'n*, 75 F.3d 1545, 1550 (Fed. Cir. 1996)).

II. CONSTRUCTION OF DISPUTED TERMS[3]

A. '929 Patent

1. "Monitoring variations in ionic current"[4]

PacBio No construction necessary
Oxford "intermittently monitoring variations in ionic current"
Court No construction necessary

The Court agrees with PacBio that the claims are not limited to intermittent monitoring. Although the word "intermittent" appears repeatedly in the specification, it is not contained in the claims. Oxford argues that the specification "consistently requires intermittent detection" so adding "intermittent" to the claims is not an improper importation of a limitation. (D.I. 92 at 16; *see also* Tr. at 12, 14) Oxford is not arguing that its construction is required due to express lexicography, disclaimer, or disavowal. (*See* Tr. at 16)

While many (possibly all) embodiments of the invention discussed in the specification involve intermittent detection, nothing in the patent (including the use of "present invention" and "invention" language) excludes the possibility of consistent, non-intermittent methods of

[3] In the attached order, the Court also adopts the parties' agreed-upon constructions for other terms.

[4] This term appears in claim 1 of the '929 patent.

"monitoring variations in ionic current."[5] "Absent a clear disavowal or contrary definition in the specification or the prosecution history, the patentee is entitled to the full scope of its claim language." *Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004). The Court is not persuaded that the specification disavows or disparages consistent, non-intermittent monitoring.

2. "Polynucleotide"[6]

PacBio "a molecule having multiple nucleotides"
Oxford "a double-stranded nucleic acid molecule comprising a first terminal portion, an intermediate portion, and a second terminal portion wherein at least a first linker ligated to the first terminal portion of the nucleic acid molecule connects a 3' terminus at the first terminal portion with a 5' terminus at the first terminal portion"
Court "a molecule having multiple nucleotides"

Oxford does not dispute that PacBio's proposed construction provides the plain meaning of "polynucleotide." (*See* Tr. at 33) Rather, Oxford argues that PacBio should be held to its previous representations to the Court when successfully opposing Oxford's motion to dismiss pursuant to 35 U.S.C. § 101 in the 17-1353 action, because claim constructions must be applied consistently for purposes of both invalidity and infringement. (*See* D.I. 127 at 15-16)

In its brief opposing Oxford's motion to dismiss, PacBio discussed the claims' "novel method of manipulating polynucleotides" by using "novel nucleic acid templates." (C.A. No. 17-

[5] Hence, the Court does not view the patent here as analogous to the one considered in *UltimatePointer, L.L.C. v. Nintendo Co.*, 816 F.3d 816, 824 (Fed. Cir. 2016).

[6] This term appears in claim 1 of the '929 patent.

1353 D.I. 24 at 1-2, 12) In the Court's opinion denying the motion to dismiss, the Court relied on these representations – but the Court was discussing the asserted claims as a whole, particularly the novelty of the methods, rather than this particular claim term.[7] Moreover, the parties had not asked the Court to construe any claim terms in connection with the § 101 motion, and the Court did not adopt any definition of "polynucleotide" or limit it to the invention's novel concept.

PacBio has consistently asserted that the claimed invention manipulates polynucleotides to create novel templates, but does not begin with novel templates of polynucleotides. Nothing stated by PacBio in connection with the motion to dismiss, nor by the Court in denying that motion, alters that fact. Here, then, the Court is persuaded that a person of ordinary skill in the art ("POSA") would understand that the term "polynucleotide" is intended to be broad and have its (undisputed) plain and ordinary meaning.

3. "nucleotide sequence"[8]

PacBio
"information reflecting the identity and order of each of the bases"

[7] *See* C.A. No. 17-1353 D.I. 48 at 11-12 ("The asserted claims provide 'a novel method of manipulating polynucleotides to create sequencing templates that can be used to generate redundant sequencing information and improve nanopore sequencing.' (D.I. 24 at 12) (citing Compl. at 16-19) The method requires introducing the polynucleotide to a system comprising a nanopore in a membrane, whereby a voltage is applied across the membrane, the variations in current are monitored, and the information from one strand is analyzed against the information from the complementary strand for improved accuracy. (See '929 patent, cl. 1) Oxford's contention that the claims are merely directed to the abstract idea of comparing and the natural phenomenon of complementarity of nucleotides ignores almost all of the content of the claim, including most of its limitations.").

[8] This term appears in claim 1 of the '929 patent.

Oxford "the identity and order of each of the bases"
Court "the identity and order of each of the bases"

There are two issues pertaining to this term: PacBio's concern regarding error rates and Oxford's concern regarding raw data. With respect to error rates, the parties agree that the term must account for the fact that nucleotide sequencing in the real world is not perfect, so the determined identity and order of bases must account for some degree of error. (*See* Tr. at 40-45) Oxford's representation that its construction is not intended to exclude errors made in determining a nucleotide sequence (*see id.* at 43-45) resolves PacBio's concern.

Oxford contends that PacBio's proposed construction would allow Plaintiff to argue that the term refers to the underlying raw data that reflects the actual base calls rather than the base calls themselves. (*See id.* at 44-45, 48) At oral argument, PacBio did not persuasively disclaim such an argument. The Court agrees with Oxford that the "nucleotide sequence" must be the base calls themselves (i.e., A, C, G, or T), not the underlying data that reflects the identity of the base calls. This conclusion is supported by the patent's specification, which distinguishes "sequence read ***data***," which is "representative of the nucleotide sequence," from "the actual ***sequence*** of the template nucleic acid molecule," noting the two "may not be identical." ('929 patent at 61:38-42) (emphasis added) PacBio's construction would improperly expand the term to include irrelevant "information." (*See* D.I. 92 at 18-19) Accordingly, the Court will adopt Oxford's proposed construction.

4. "The sequence of the template nucleic acid"[9]

PacBio "information reflecting the identity and order of each of the bases of the template nucleic acid"
Oxford "the identity and order of each of the bases of the template nucleic acid"
Court "the identity and order of each of the bases of the template nucleic acid"

The arguments presented with respect to this term are essentially identical to the arguments presented with respect to the term "nucleotide sequence," discussed just above. For the same reasons stated there, the Court will adopt Oxford's proposed construction.

5. "redundant sequence information"[10]

PacBio No construction necessary
Oxford "information that includes the identity and order of each of the bases of the complementary strands"
Court No construction necessary

The claim provides that "the redundant sequence information comprises the nucleotide sequence of the complementary strands" ('929 patent, cl. 1), and the Court has already held that "nucleotide sequence" is construed as "the identity and order of each of the bases." PacBio argues that Oxford's proposed construction for "redundant sequence information" is itself "redundant" (D.I. 91 at 6-7), to which Oxford responds that it is "entirely consistent with how the

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[9] This term appears in claim 1 of the '400 patent and claim 1 of the '323 patent.

[10] This term appears in claim 1 of the '929 patent.

claims themselves define these terms" (D.I. 127 at 18). The Court agrees that the claims and the Court's constructions already define the pertinent terms and that the further construction proposed here by Oxford would be redundant and potentially confusing.

6. "linked"[11]

PacBio No construction necessary
Oxford "covalently bonded at the 3' end of the first nucleic acid segment and the 5' end of the second nucleic acid segment"
Court No construction necessary

Claim 8 recites "[t]he method of claim 1, wherein the complementary strands are linked." ('929 patent, cl. 8) Claim 10 recites "[t]he method of claim 8, wherein the complementary strands are linked by a linker comprising a nucleotide." (*Id.*, cl. 10) The parties agree that the term "***linker***" in claim 10 should be construed as "a nucleic acid covalently bonding a 3' end of the first nucleic acid segment with a 5' end of the second nucleic acid segment." (D.I. 80 Ex. A) They dispute, however, whether "***linked***" in claim 8 is also limited to a covalent linkage. (*See* Tr. at 60, 63)

Oxford points to no intrinsic evidence to support its contention that a POSA would understand the term "linked" to refer only to covalent bonds; nothing in the patent appears to exclude other types of bonds. (*See* Tr. at 61-65) Oxford relies on an expert declaration from Dr. Patrick Hrdlicka, a POSA, who reviewed the patent and opines that a POSA reading the patent would "not understand the term 'linked' to mean anything other than a covalent bond." (D.I. 97

[11] This term appears in claim 8 of the '929 patent.

at 4, 14-16) Given the undisputed silence of the intrinsic evidence on this point (*see* Tr. at 64), Dr. Hrdlicka's (extrinsic) opinion does not persuade the Court to limit "linked" to covalent bonds.

7. "determining a consensus sequence for the region of interest"[12]

PacBio "determining the most likely actual nucleotide sequence for the region of interest"
Oxford "determining a sequence of nucleotides compiled by inserting the nucleotide occurring most often at each position in the real sequences for the region of interest"
Court "determining the most likely actual nucleotide sequence for the region of interest"

The parties' dispute the appropriate definition of "consensus sequence." PacBio's proposal slightly modifies the specification's definition of "consensus sequence data," which is "representative of a most likely actual sequence of the template nucleic acid." ('929 patent at 12:11-12) (cited at D.I. 91 at 7) Oxford argues that this is a definition of "consensus sequence ***data***," not "consensus sequence," and that the two concepts are used "distinctly and not interchangeably" in the specification. (Tr. at 74; *see also* D.I. 92 at 20) In the Court's view, deleting "representative of" from the definition of "consensus sequence data" results in an appropriate basis for a construction of "consensus sequence."

Oxford's proposed construction comes from a different part of the intrinsic record, namely a dictionary definition that was submitted with an Information Disclosure Statement during prosecution. (*See* D.I. 127 at 18) The dictionary defines "consensus sequence" as "a sequence of nucleotides or amino acids that is used to describe a number of related but not

[12] This term appears in claim 1 of the '929 patent.

identical sequences," which "is compiled by inserting the nucleotide occurring most often at each position in the real sequences." (D.I. 91 Ex. 3) While it is true that the patentee submitted this definition to the PTO, the patentee did not argue nor discuss the definition, and neither did the Examiner. (*See* Tr. at 71) Merely because a dictionary definition is part of the prosecution history does not necessarily import that definition into the claims. *See generally Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1279 (Fed. Cir. 2003) ("[M]ere submission of an IDS to the USPTO does not constitute the patent applicant's admission that any reference in the IDS is material prior art.").

PacBio further faults Oxford's construction for reading out an embodiment from the claims. According to PacBio, satisfying Oxford's requirement of a nucleotide occurring "most often" at a position requires at least three reads, so Oxford's construction would exclude embodiments that involve only two sequence reads. (Tr. at 68-69) Oxford disagrees. (*See id.* at 69, 74) (discussing '929 patent at Fig. 21A, 38:1-11) Whether the embodiment about which the parties are disagreeing is limited to two reads or allows for at least three reads is a factual dispute that need not be resolved in order to construe the claim term.

B. '400 and '323 Patent Terms

1. "N"[13]

PacBio "an integer"
Oxford "the number of bases that affect the current measurement"
Court "an integer three or greater that equals the number of monomeric units in the [pore / nanopore] that affect (i.e., vary) the current measurement of the [property / electrical signal] being measured"

The principal dispute here is whether "N" is defined by the specification, as Oxford posits. Claim 1 of the '400 patent is a method claim that comprises, in part, "measuring a property which has a value that varies for N monomeric units of the template nucleic acid in the pore, wherein the measuring is performed as a function of time, while the template nucleic acid is translocating through the nanopore, wherein N is three or greater." ('400 patent, cl. 1)[14] The '400 patent's specification has a subsection entitled "Base Calling Methods" whose first paragraph reads:

> Nanopore sequencing generally does not achieve single nucleotide resolution, especially in embodiments that might be scaled to a commercially viable DNA sequencing system. Rather, the

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[13] This term appears in claim 1 of the '400 patent and claim 1 of the '323 patent.

[14] Claim 1 of the '323 patent similarly is a method that comprises, in part, "measuring an ***electrical signal*** which has a value that varies for ***at least*** N monomeric units of the template nucleic acid in the ***nanopore***, wherein the measuring is performed as a function of time while the template nucleic acid translocates through the nanopore, wherein N is three or greater." ('323 patent, cl. 1) (emphasis added to show language slightly different from claim 1 of '400 patent) The Court finds that the slight differences between the language in the two claims does not impact the claim construction analysis. As the '400 and '323 patents have similar specifications and claim language, the Court will focus its discussion on the '400 patent.

> amplitude of electric current passing through the nanopore (which constitutes the signal) depends on the identity of the several bases that reside in the pore throughout the duration of the current measurement. Thus, rather than there being 4 distinct current levels (for A, G, C, T) when the ssDNA translocates through the nanopore, there are 4 to the N levels (***N=the number of bases that affect the current measurement***), some of which may be degenerate (see FIG. 28). Furthermore, the bases residing in the center of the nanopore likely affect the current measurement more than those near the entrance or exit.

(*Id.* at 39:48-62) (emphasis added)

PacBio argues that the claim defines "N" so no construction is necessary beyond clarifying that "N" refers to an integer (whole number) rather than a decimal or fraction – a basic concept that is undisputed. (*See* D.I. 91 at 10) The Court agrees, instead, with Oxford that PacBio's construction would not be helpful to the jury and, more importantly, that further elaboration of the limitations of N is necessary to resolve the parties' dispute. (*See* D.I. 92 at 12)

At oral argument, PacBio explained that "[t]he claims tell you what the values of N can be" – that is, "a number of nucleotides for which the property you are measuring varies," "three or greater" – and include only those nucleotides "that are actually in the pore." (Tr. at 86) Oxford argues that the definition of "N" is, instead, defined in the clear lexicography of the specification, which provides that "N=the number of bases that affect the current measurement." (*See* D.I. 92 at 12)

As both parties acknowledge, the specification paragraph reproduced above explains the general concept that, rather than there being one current level associated with each of the four types of bases (i.e., four total current levels), "the total number of current levels is in fact based on the total number of nucleotides that affect the measurement." (Tr. at 88; *see also id.* at 98) In

other words, "the current level that is passing through the nanopore depends on the identity of the several bases that reside in the pore throughout the duration of the measurement." (*Id.* at 87-88; *see also* D.I. 127 at 9-10) Thus, N, in the specification, is used to calculate "how many different possible current levels there can be." (*Id.* at 90; *see also id.* at 104; D.I. 127 at 9) Neither party disputes these facts.

The dispute arises from PacBio's contention that in the claim, "the signal has to ***vary*** for N units . . . [a]nd that is a subset of the number of nucleotides that ***affects*** the measurement." (Tr. at 106) (emphasis added) The fact that the claim requires the property to "vary" means, according to PacBio, that "[t]hat is a constraint on N," such that "[y]ou can't choose a value of N for which the property doesn't vary." (*Id.* at 94) For example, according to PacBio, while ten monomeric units may "affect" the measurement, it is possible that only five of those actually "vary" the measurement, in which instance N (in the claim) would be equal to five. (*See id.* at 89-90)

Oxford argues that PacBio's position "that N can be a subset of the units that affect the current measurement is nowhere in the specification." (*Id.* at 107; *see also id.* at 98) While the specification makes clear that "the bases residing in the center of the nanopore likely affect the current measurement more than those near the entrance or exit" ('400 patent at 39:60-62), all of those bases are still in the pore and "affect[ing] the current measurement." Indeed, the patent expressly states that the measurement of the electric current "depends on the identity of the several bases that reside in the pore throughout the duration of the current measurement." (*Id.* at 39:52-55) There is nothing in the intrinsic record showing that the patentee intended to draw a line between bases in the pore that largely affect (or vary) the measurement and those that affect

the measurement to a lesser extent.[15] (*See* Tr. at 101)

PacBio further insists that "you can cho[o]se any value of N so long as the signal varies for those Ns." (*Id.* at 94-95) The claim, however, does not state that a POSA can ***choose*** any value for N; rather, the method requires that one measure a property that "***has*** a value" at a specific time based on precisely "N monomeric units . . . in the pore."

In sum, the Court is not persuaded by PacBio that "vary" means something different from "affects" or "impacts" or "contributes to." (*See id.* at 104-06) (PacBio using terms "contributing to," "possibly impacting," "really impacting," "varies," and "affect[ing]") If certain bases do not "affect," "impact," "contribute to," or "vary" the "value" of the property being measured at a particular point in time, then those bases are not counted toward N. On the other hand, N must count all bases that do affect, impact, contribute to, or vary the value of the property being measured at a point in time.

The Court's conclusion is consistent with the prosecution history. The patentee distinguished the invention from prior art Hibbs on the ground that Hibbs was not using 4^N combinations of possible current levels. (*See id.* at 92; D.I. 80 Ex. G at 5) The prosecution history's discussion of Hibbs confirms that N refers to the total number of "bases within the pore [that] are contributing to the signal." (D.I. 92 at 12; *see also* Tr. at 100) Indeed, as the patentee noted during prosecution, "[t]he instant inventors discovered that in order to obtain reliable sequence information, one first has to understand how many bases within the pore are contributing to the signal (N)." (D.I. 80 Ex. G at 5) The patentee consistently referred to N as

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[15] Such a line might also raise indefiniteness concerns. It is preferable to construe a term "to avoid invalidity on indefiniteness grounds." *Power-One, Inc. v. Artesyn Techs., Inc.*, 599 F.3d 1343, 1350 (Fed. Cir. 2010).

the number of bases in the pore contributing to the signal. PacBio has not shown that the patentee intended to add an additional limitation to the claim by using the term "varies" instead of "affects" or "contributing to."

The Court adopts a construction that adheres to both the definition of "N" in the specification and the further limitations provided in the claims. Accordingly, the Court construes "N" as "an integer three or greater that equals the number of monomeric units in the [pore / nanopore] that affect (i.e., vary) the current measurement of the [property / electrical signal] being measured."

2. "calibration information produced by measuring such property for 4 to the N sequence combinations"[16]

PacBio No construction necessary
Oxford "calibration information generated by measuring the property for each of the 4^N possible combinations of nucleotides"
Court "calibration information produced by measuring the property for each of the 4^N possible combinations of nucleotides"

At oral argument, Oxford conceded that "generated by" and "produced by" are synonymous, and the parties agreed to a slightly revised version of Oxford's construction, which the Court will adopt. (*See* Tr. at 110, 115)

[16] This term appears in claim 1 of the '400 patent.

3. "calibration information that accounts for the electrical signal for 4 to the N sequence combinations"[17]

PacBio No construction necessary
Oxford "calibration information generated by measuring the property for each of the 4^N possible combinations of nucleotides"
Court No construction necessary

The parties disagree over whether the prosecution history limits the calibration information to being measured, or whether the calibration information may also be determined experimentally or calculated, as expressly provided in dependent claims 6 and 7, respectively. Oxford argues that because Hibbs discloses only a subset of 4^N measurements and the patentee distinguished Hibbs, the patentee must have disclaimed anything other than producing calibration information by measuring the property. (*See* Tr. at 111-12) The Court is not persuaded, for reasons including that Oxford's proposed construction would improperly exclude dependent claims 6 and 7. The intrinsic record supports the conclusion that there are multiple ways of determining the calibration information, and no construction of the disputed term is necessary.

[17] This term appears in claim 1 of the '323 patent.

4. "in the pore" / "in the nanopore"[18]

PacBio No construction necessary
Oxford "between the entrance and exit of the nanopore"
Court No construction necessary

The parties dispute whether these terms need to be construed or whether issues related to them should be dealt with at the infringement stage. At oral argument, both parties stated that they intend to apply the plain and ordinary meaning of "in the pore." (*See* Tr. at 123, 126) While Oxford anticipates that a dispute may arise later in this case as to whether certain portions of space between the entrance and exit of an irregularly-shaped nanopore are in the pore, the Court concludes that this is a question of fact to be resolved (if need be) in connection with any infringement analysis (after discovery is complete). *See Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 442 F.3d 1322, 1326 (Fed. Cir. 2006).

C. '056 Patent Term: "Kinetic step"[19]

PacBio "a reaction step that can be associated with a rate constant"
Oxford Indefinite
Court Indefinite

[18] "In the pore" appears in claim 1 of the '400 patent and "in the nanopore" appears in claim 1 of the '323 patent.

[19] This term appears in claim 1 of the '056 patent.

Pursuant to 35 U.S.C. § 112, "a patent's claims, viewed in light of the specification and prosecution history, [must] inform those skilled in the art about the scope of the invention with reasonable certainty." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2129 (2014); *see also Cox Commc'ns, Inc. v. Sprint Commc'n Co. LP*, 838 F.3d 1224, 1231 (Fed. Cir. 2016) (noting relevant inquiry is "whether the 'claims,' not particular claim terms" inform one of scope with reasonable certainty). "Indefiniteness must be proven by clear and convincing evidence." *Sonix Tech. Co., Ltd. v. Publications Int'l, Ltd.*, 844 F.3d 1370, 1377 (Fed. Cir. 2017).

Claim 1 of the '056 patent requires that "the translocating enzyme and the reaction conditions are selected such that the translocating enzyme exhibits two kinetic steps wherein each of the kinetic steps has a rate constant, and the ratio of the rate constants of the kinetic steps is from 10:1 to 1:10." The parties' dispute concerns whether the claims require that a POSA can precisely determine the number of kinetic steps in a given reaction and each step's corresponding rate constants. The Court concludes that the claims require a POSA to be able to determine the number of kinetic steps and each step's rate constant, but a POSA would not be able to do so with reasonable certainty.

The specification describes the present invention as "a sequence of steps, wherein each step can be characterized as having a particular forward and reverse reaction rate that can be represented by a rate constant." ('056 patent at 25:35-38) The patent further provides that there is no "unique representation of the process" as the biochemical process is "relatively complex" and is described only in "a simplified schematic fashion." (*Id.* at 25:32-34, 25:40-41) Thus, as is undisputed, one enzymatic process may be "described using fewer steps" or alternatively "represented by including additional steps." (*Id.* at 25:41-45; *see also id.* at 25:51-55; Tr. at 146)

Oxford has demonstrated by clear and convincing evidence that the term "kinetic step" is indefinite because "there are an indeterminate number and type of kinetic steps for a given enzymatic process," even as the claim language makes it "imperative to know the rate constants of all the steps." (D.I. 127 at 1) The claim is indefinite also because the required "ratio of the rate constants of the kinetic steps" ('056 patent, cl. 1) "depends arbitrarily on the representation considered" (D.I. 92 at 3). Thus, "it is entirely possible that the ratio of the rate constants for any two steps may fall within the claimed range in one representation, but not in the other." (D.I. 127 at 6; *see also* D.I. 92 at 5) For example, two POSAs could each graphically represent a given enzymatic reaction differently – each with a different number of steps and, therefore, different rate constants and resulting ratios – and one POSA's graphic representation shows infringement while the other's does not, even though they are characterizing (differently) the very same reaction. (*See* Tr. at 134-36) PacBio's argument that the "enzyme will still exhibit the same kinetic behavior, and . . . produce the same results" (D.I. 124 at 16) is true but unavailing because the claim requires that the enzymatic reaction be able to be characterized in terms of a precise number of steps.

Accordingly, the Court concludes that this term is indefinite.

D. "Nanopore"[20]

PacBio "an opening sized so that the passage of a molecule through the opening can be detected by a change in a signal"
Oxford "a nanometer-sized hole"
Court No construction necessary

At oral argument, the parties agreed that no construction is necessary for this term. (*See* Tr. at 157-58)

III. CONCLUSION

The Court construes the disputed and undisputed terms as explained above. An appropriate Order follows.

[20] This term appears in all of the patents.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,	:	
Plaintiff,	:	
v.	:	C.A. No. 17-275-LPS-CJB
	:	C.A. No. 17-1353-LPS-CJB
OXFORD NANOPORE TECHNOLOGIES, INC. and OXFORD NANOPORE TECHNOLOGIES, LTD.,	:	
Defendants.	:	

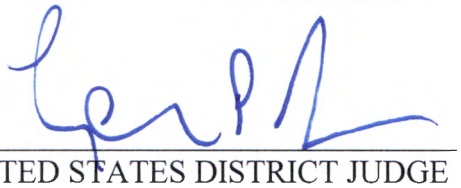
ORDER

At **Wilmington**, this **6th** day of **March, 2019**:

For the reasons set forth in the Memorandum Opinion issued this date, **IT IS HEREBY ORDERED** that the claim terms in this case are construed as follows:

Claim Term	**Court's Construction**
"enzyme chaperone-regulated passage of the polynucleotide through the nanopore"	"enzyme-guided movement of the polynucleotide through the nanopore"
"linker"	"a nucleic acid covalently bonding a 3' end of the first nucleic acid segment with a 5' end of the second nucleic acid segment"
"monitoring variations in ionic current"	No construction necessary
"polynucleotide"	"a molecule having multiple nucleotides"
"nucleotide sequence"	"the identity and order of each of the bases"
"the sequence of the template nucleic acid"	"the identity and order of each of the bases of the template nucleic acid"
"redundant sequence information"	No construction necessary
"linked"	No construction necessary

"determining a consensus sequence for the region of interest"	"determining the most likely actual nucleotide sequence for the region of interest"
"N"	"an integer three or greater that equals the number of monomeric units in the [pore / nanopore] that affect (i.e., vary) the current measurement of the [property / electrical signal] being measured"
"calibration information produced by measuring such property for 4 to the N sequence combinations"	"calibration information produced by measuring the property for each of the 4^N possible combinations of nucleotides"
"calibration information that accounts for the electrical signal for 4 to the N sequence combinations"	No construction necessary
"in the pore" / "in the nanopore"	No construction necessary
"kinetic step"	Indefinite
"nanopore"	No construction necessary



UNITED STATES DISTRICT JUDGE