

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Plaintiff,

vs.

OXFORD NANOPORE TECHNOLOGIES, INC.

Defendant.

Civil Action No. _____

JURY TRIAL DEMANDED

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Pacific Biosciences of California, Inc. (“Plaintiff” or “PacBio”) for its complaint against Defendant Oxford Nanopore Technologies, Inc. (“Oxford”) alleges and states the following:

NATURE OF THE ACTION

1. This is an action for patent infringement arising under the United States Patent Act, 35 U.S.C. §§1, *et seq.*, including 35 U.S.C. § 271.
2. PacBio brings this action to halt Oxford’s infringement of PacBio’s rights under the Patent Laws of the United States 35 U.S.C. § 1, *et seq.*, which arise under U.S. Patent No. 9,546,400 (“the ’400 patent”) (attached as Exhibit 1).

THE PARTIES

3. PacBio is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 1305 O’Brien Drive, Menlo Park, California 94025.
4. PacBio was founded in the year 2000 and develops, manufactures, and sells a novel DNA sequencing platform that helps researchers resolve genetically complex problems.

PacBio's DNA sequencing technology is based on real-time detection of the incorporation of nucleotides into a single strand of DNA. That technology goes by the name "SMRT®" sequencing, which is short for "Single Molecule, Real-Time" sequencing. PacBio's SMRT® sequencing platform encompasses not just DNA sequencing instruments, but also novel sequencing chips and chemical reagents for use with PacBio's DNA sequencing instrument and sophisticated software for analyzing the data that emerges from PacBio's sequencing instruments.

5. PacBio's SMRT® Sequencing Platform and technology allows researchers to carry out numerous applications, including at least (1) de novo genome assembly to finish genomes in order to more fully identify, annotate, and decipher genomic structures; (2) targeted sequencing to more comprehensively characterize genetic variations; and (3) identification of DNA base modifications to help characterize epigenetic regulation and DNA damage. PacBio's SMRT® Sequencing Platform and technology provides high accuracy, ultra-long reads, uniform coverage, and is believed to be the only DNA sequencing technology that provides the ability to simultaneously detect epigenetic changes.

6. In addition to the commercialization of its flagship SMRT® sequencing platform, PacBio has broad expertise in single-molecule sequencing and is engaged in exploratory work related to single-molecule sequencing, including techniques related to single-molecule sequencing based on detection platforms such as nanopores. Collectively, PacBio's research and development efforts have resulted in a patent portfolio that includes over 330 issued U.S. patents and pending applications related to single-molecule sequencing techniques.

7. Defendant Oxford is a corporation organized under the laws of Delaware with its principal place of business at 1 Kendall Square, Bldg. 200, Cambridge, Massachusetts 02139.

On information and belief, Oxford is engaged in the commercialization throughout the United States of nanopore-based single-molecule sequencing products, including at least the MinION and PromethION sequencing instruments and reagents and kits for use with these instruments.

JURISDICTION AND VENUE

8. This action arises under the Patent Laws of the United States, Title 35, United States Code, §§ 1 *et seq.*, including 35 U.S.C. §§ 271 and 281.

9. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

10. This Court has personal jurisdiction over defendant Oxford. Oxford has substantial contacts with the forum as a consequence of conducting business in Delaware, and has purposefully availed itself of the benefits and protections of Delaware state law by incorporating under Delaware law.

11. Venue is proper in this District under 28 U.S.C. §§ 1391(b) and (c), and 1400(b) because Oxford is a Delaware corporation and Delaware is a convenient forum for resolution of the parties' disputes set forth herein.

BACKGROUND

12. On information and belief, in the 2015 timeframe Oxford began commercializing single-molecule sequencing products based on the use of protein nanopores. Oxford purports to offer a single-molecule sequencing product that, like PacBio's products, are capable of determining the sequence of long stretches of DNA in a single pass. The ability to generate such "long reads" is an area where PacBio has and continues to be widely recognized as the technical and commercial leader. PacBio and Oxford compete in the single-molecule sequencing market.

13. Oxford's single-molecule sequencing products include at least the MinION and PromethION sequencing instruments and reagents, consumables, and software for use with same.

Two views of a representative MinION device are shown below:

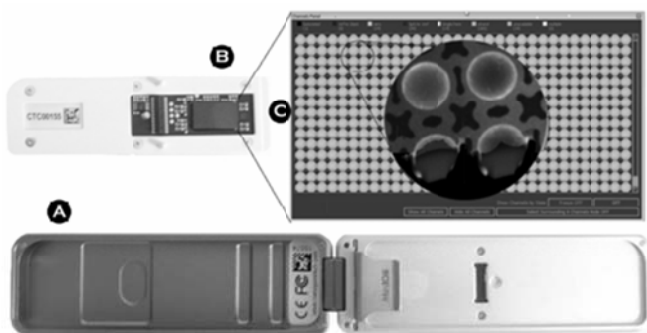
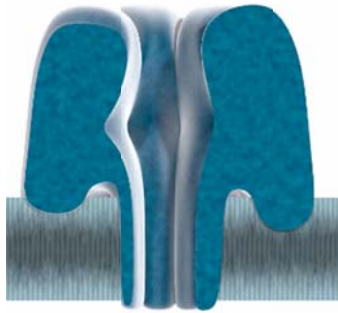


Figure 4. (A) MinION MkI (B) flow cell (C) nanopore array (Individual nanopore cells reproduced, modified, with permission from Oxford Nanopore).

Exhibit 3; Exhibit 4 at 292. The top image shows a working MinION device, and the bottom view shows the interior of the device. The portion labeled “C” in the above photograph depicts a flow cell with an array of individual nanopores. Nanopores are tiny holes embedded into a membrane and are formed by inserting proteins that have a hollow tube through their center into a polymer membrane, as shown in the image below:



See Exhibit 5. The Accused Products each include one or more flow cells that include a “nanopore array.”

14. While the MinION instrument includes a single flow cell, the PromethION instrument includes 48 flow cells and has been described as a “whole box of MinION sequencers.” Exhibit 6. A representative PromethION instrument with its 48 flow cells is shown below:



Id.

15. To sequence DNA using Oxford's products, one first applies a voltage across the membrane such that an electrical current flows through the hole. A strand of DNA is then drawn through the hole:



Exhibit 7. As the DNA passes through the hole, it disrupts the electrical current that is passing through the hole, thus producing a signal. To evaluate the sequence, one can attempt to correlate this signal with the DNA bases that are passing through the hole.

16. More particularly, in nanopore-based DNA sequencing systems, such as those sold by Oxford, the signal that results from passage of the DNA through the nanopore arises not just from a single DNA base, but from a contiguous group of DNA bases that interacts with the nanopore at a given time. Therefore, to determine the DNA sequence, Oxford nanopore uses calibration information produced by measuring the signals from the different combinations of bases that may interact with the nanopore at a given time.

17. Oxford infringes, literally or under the doctrine of equivalents, PacBio's '400 patent through its activities connected to at least the MinION and/or the PromethION instruments. For instance, representative claim 1 of the '400 patent is listed below:

1. A method for sequencing a nucleic acid template comprising:
 - a) providing a substrate comprising a nanopore in contact with a solution, the solution comprising a template nucleic acid above the nanopore;
 - b) providing a voltage across the nanopore;
 - c) 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; and
 - d) determining the sequence of the template nucleic acid using the measured property from step (c) by performing a process including comparing the measured property from step (c) to calibration information produced by measuring such property for 4 to the N sequence combinations.

18. Use of Oxford's sequencing products leads to direct infringement of this claim in the following way. First, Oxford's products include nucleic acid sequencing instrument having a nanopore-containing membrane that is in contact with a solution (step a). A voltage is then applied across the membrane to drive a current across the membrane (step b). A nucleic acid molecule to be sequenced is then drawn through the nanopore, and, as a result, the current is disrupted in a time-dependent manner that varies based on the N (wherein N is three or greater) monomeric nucleic acid bases that are interacting with the pore at a given time (step c). An artificial neural network is then used to compare the signal obtained from drawing the nucleic acid through the nanopore to calibration information obtained from measuring such a signal from the 4 to the N combinations of bases, thus allowing one to determine the sequence of the nucleic acid (step d).

19. As an example, attached hereto as Exhibit 2 is a preliminary and exemplary claim chart detailing Oxford's infringement of multiple claims of the '400 patent. This chart is not intended to limit PacBio's right to modify the chart or allege that other activities of Oxford infringe the identified claims or any other claims of the '400 patent or any other patents. Exhibit 2 is hereby incorporated by reference in its entirety. Each claim element in Exhibit 2 that is

mapped to Oxford's MinION and/or PromethION instruments shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

COUNT I

(Infringement of U.S. Patent No. 9,546,400)

20. Plaintiff repeats and re-alleges each and every allegation contained in the preceding paragraphs of this Complaint as if stated in their entirety herein, and incorporates them herein by reference.

21. The '400 patent, entitled "Nanopore Sequencing Using N-mers," issued on January 17, 2017, to inventors Steven Turner and Benjamin Flusberg. The '400 patent is assigned on its face to Plaintiff PacBio. PacBio is the owner of all rights, title to and interest in the '400 patent.

22. On information and belief, Oxford has infringed and continues to infringe at least claims 1-8, 10, and 14-15 of the '400 patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by using within the United States without authority the MinION and/or the PromethION instruments. As an example, attached as Exhibit 3 is a preliminary and exemplary claim chart detailing Oxford's infringement of these claims of the '400 patent. This chart is not intended to limit PacBio's right to modify the chart or allege that other activities of Oxford infringe the identified claims or any other claims of the '400 patent or any other patents. Exhibit 3 is hereby incorporated by reference in its entirety. Each claim element in Exhibit 2 that is mapped to Oxford's MinION and/or PromethION instruments shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

23. Oxford has had knowledge of and notice of the '400 patent and its infringement long before the filing of this complaint. For instance, on March 21, 2016, Oxford cited PacBio's U.S. Patent Application Publication No. 2010/0331194 in an information disclosure statement during prosecution of Oxford's U.S. Patent Application No. 13/147,159. *See* Ex. 12 at 5. The application that published as PacBio's Publication No. 2010/0331194 is the parent of the application that issued as the '400 patent, and as such shares the same specification as the '400 patent. On information and belief, Oxford has monitored PacBio's patent filings and has been aware of the '400 patent since its issuance on January 17, 2017. At a minimum, Oxford has had knowledge of and notice of the '400 patent and its infringement since at least, and through, the filing and service of PacBio's complaint in this action and despite this knowledge continues to commit the aforementioned infringing acts.

24. Oxford actively, knowingly, and intentionally has induced, or has threatened to induce, infringement of at least claims 1-8, 10, and 14-15 of the '400 patent through a range of activities. First, on information and belief, Oxford has induced infringement by controlling the design and manufacture of, offering for sale, and selling the MinIon and/or PromethION instruments with the knowledge and specific intent that its customers will use these instruments to infringe, literally or under the doctrine of equivalents, by performing the claimed method for sequencing a nucleic acid template. For instance, Oxford has admitted in an ongoing International Trade Commission investigation that it imports, sold for importation, and or/sells its MinION product and PromethION product within the United States. *See* Ex. 8 ¶ 53.

25. Second, on information and belief, Oxford has induced infringement by its customers through the dissemination of promotional and marketing materials relating to the MinION and/or PromethION instruments with the knowledge and specific intent that its

customers will use these instruments to infringe, literally or under the doctrine of equivalents, by performing the claimed method for sequencing a nucleic acid template. For instance, Oxford promotes the MinION and/or PromethION instruments on its website, stating that its products offer numerous benefits such as real-time DNA/RNA sequencing, no capital cost, long reads, scalability, high-fidelity, and rapid library preparation time. *See* Ex. 9.

26. Third, on information and belief, Oxford has induced infringement by its customers through the creation of distribution channels for the MinION and/or PromethION instruments in the United States with the knowledge and specific intent that its customers will use these instruments to infringe, literally or under the doctrine of equivalents, by performing the claimed method for sequencing a nucleic acid template. For instance, Oxford's website allows customers in the United States to purchase starter packs for Oxford's MinION instruments that, when used, will lead to infringement of the '400 patent. As Oxford's website states, "[b]uy a Starter Pack to join the growing numbers in the Nanopore Community." *See* Ex. 10. As another example, Oxford has created an early access program for its PromethION instrument that provides access to a PromethION device, site installation support, flow cells and reagents, and further information and support. *See* Ex. 11.

27. Fourth, on information and belief, Oxford has induced infringement through the distribution of other instructional materials, product manuals, and technical materials with the knowledge and the specific intent to encourage and facilitate its customer's infringing (either literally or under the doctrine of equivalents) use of MinION and/or PromethION instruments. Oxford is liable for its induced infringement of the '400 patent pursuant to 35 U.S.C. § 271 (b).

28. Oxford has contributed to, or has threatened to contribute to, the infringement by its customers of the '400 patent by, without authority, selling and offering to sell within the

United States materials and apparatuses for practicing the claimed invention of the '400 patent, including at least the MinION and PromethION instruments. When, for example, either of these instruments is used by Oxford's customers for nucleic acid sequencing, the claimed method of the '400 patent for sequencing a nucleic acid template is performed, thereby infringing, literally or under the doctrine of equivalents, at least claims 1-8, 10, and 14-15 of the '400 patent.

29. On information and belief, Oxford knows that the MinION and PromethION instruments constitute a material part of the inventions of the '400 patent and that they are not a staple article or commodity of commerce suitable for substantial noninfringing use. As documented above, the MinION and PromethION instruments consist of specialized substrates containing protein nanopores that are used in conjunction with specialized reagents for the purpose of sequencing nucleic acid templates. *See supra* ¶¶ 12 - 19. As such, neither the MinION nor PromethION instruments nor any of the reagent kits for use with these instruments is a staple article of commerce suitable for substantial non-infringing use. Oxford knows that these instruments are not staple articles or commodities of commerce suitable for substantial non-infringing use because they have no use apart from infringing the '400 patent. Oxford is liable for its contributory infringement of the '400 patent pursuant to 35 U.S.C. § 271(c).

30. Oxford's infringement of the '400 patent has injured PacBio in its business and property rights. PacBio is entitled to recover monetary damages for such injuries pursuant to 35 U.S.C. § 284 in an amount to be determined at trial. Oxford's infringement of the '400 patent has caused irreparable harm to Plaintiffs and will continue to cause such harm unless and until Oxford's infringing activities are enjoined by this Court.

PRAYER FOR RELIEF

WHEREFORE, prays for relief as follows:

- A. Judgment that Oxford has infringed the '400 patent;
- B. An order permanently enjoining Oxford from further infringement of the '400 patent;
- C. An award of damages pursuant to 35 U.S.C. § 284 plus pre-judgment and post-judgment interest;
- D. An award to PacBio of its costs and reasonable expenses to the fullest extent permitted by law;
- E. A declaration that this case is exceptional pursuant to 35 U.S.C. § 285, and an award of attorneys' fees and costs; and
- F. An award of such other and further relief as the Court may deem just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Federal Rule of Civil Procedure 38(b), PacBio hereby demands a trial by jury on all issues so triable.

Dated: March 15, 2017

Respectfully submitted,

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