

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference N.102405B CHM	FOR FURTHER ACTION		See item 4 below
International application No. PCT/GB2008/004127	International filing date (<i>day/month/year</i>) 15 December 2008 (15.12.2008)	Priority date (<i>day/month/year</i>) 19 December 2007 (19.12.2007)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant OXFORD NANOPORE TECHNOLOGIES LIMITED			

<p>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
<p>3. This report contains indications relating to the following items:</p> <table border="0"> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> <p>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</p>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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	Date of issuance of this report 22 June 2010 (22.06.2010)
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)**

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION.
See paragraph 2 below

International application No.
PCT/GB2008/004127

International filing date (day/month/year)
15.12.2008

Priority date (day/month/year)
19.12.2007

International Patent Classification (IPC) or both national classification and IPC
INV. G01N33/487 B01D67/00

Applicant
OXFORD NANOPORE TECHNOLOGIES LIMITED

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**


If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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D-80298 Munich
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Date of completion of this opinion

see form
PCT/ISA/210

Authorized Officer

Johnson, Keith

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - the international application in the language in which it was filed
 - a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - on paper
 - in electronic form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in electronic form.
 - furnished subsequently to this Authority for the purposes of search.
4. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. IV Lack of unity of invention

1. In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- paid additional fees
 - paid additional fees under protest and, where applicable; the protest fee
 - paid additional fees under protest but the applicable protest fee was not paid
 - not paid additional fees
2. This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- complied with
 - not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- all parts.
 - the parts relating to claims Nos. 1-71

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>3, 9-10, 14-16, 35-36, 45-47, 64-67</u>
	No: Claims	<u>1-2, 4-8, 11-13, 17-34, 37-44, 48-63, 68-71</u>
Inventive step (IS)	Yes: Claims	<u>3, 15-16</u>
	No: Claims	<u>1-2, 4-14, 17-71</u>
Industrial applicability (IA)	Yes: Claims	<u>1-71</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Section IV. Lack of unity of invention

1 Document:

DNU = EP 1 669 746 A1

is a prior art document describing the preparation of lipid bilayer membranes (BLMs) and their use in electrophysiological measurements, especially single ion channel recordings (cf. DNU, abstract; figure 1). In particular, an apparatus is described which comprises elements defining a chamber (3), the elements including a body (9) of non - conductive material having formed therein a recess (8) opening into the chamber and containing an electrode (16). The subject matter of claims 1 - 14, 17 - 45, 48 - 63, to the extent that it is new and inventive, differs from this prior art essentially by the pretreatment of the body to render it hydrophobic. By these means, the applicants solve the problem of ' ... *providing highly resistive seals having an electrical resistance of 1G Ω* thereby enabling ' ... *stochastic recordings from single protein pores...*' (cf. present application, page 3, lines 15 - 19; 25 - 34). So these features represent the contribution made by the applicants over the prior art and constitute a first set of special technical features, STF₁ say, in the sense of **Rule 13.2 PCT**.

2 In contrast, the subject matter of claims 64 - 71 differs from the same prior art by providing a conductive polymer, especially polypyrrole, on the electrode. This has the advantage of increasing ' ... *the charge reservoir available to the electrodes...*' thereby stabilising the performance of the electrode (cf. present application, page 9, lines 30 - 34). Hence these features constitute a second group of special technical features, STF₂. Claims 15, 16, 46, and 47 naturally fall within this group of inventions.

3 A comparison of the sets of special technical features, STF₁ and STF₂ shows them to be different. Moreover, they solve different technical problems. So they neither complement nor correspond to one another. Therefore the technical relationship required by **Rule 13.1 PCT** for unity of invention does not exist between the two groups of claims. Consequently, in the view of the International Searching Authority, the current application contains two inventions which are not so linked as to form a single, general inventive concept.

Section V. Reasoned statement under Rule 43bis.1(a)(i) PCT

INVENTION 1

- 1 In any case, the subject matter of the independent apparatus claim, claim 30, has already been anticipated by the disclosure of the following documents:

D1 = REVIEWS IN MOLECULAR BIOTECHNOLOGY, vol. 74,1
January 2000 (2000-01-01) , pages 159-174, XP001059471 ISSN:
1389-0352; CHENG Y et al: "Discrete membrane arrays"

D2 = WO 94/25862 A1

D3 = EP 1 712 909 A1,

because each of these documents teaches an apparatus for supporting a layer separating two volumes of aqueous solution comprising:

- elements defining a chamber, the elements including a body of non-conductive material (eg. SU8 photoresist in D1; silicon or polyimide in D2; parylene coated silicon in D3) having formed therein at least one recess opening into the chamber; and
- an electrode contained in the recess. This is confirmed by reference to the passages cited in the search report, viz. D1, page 169, right-hand column, paragraph 2 ' *The most popular methods...*' - page 173, right-hand column, paragraph 3 ' *... stable bilayer based sensor*'; figures 13, 14; D2 page 5, line 8 - page 11, line 6; figures 1, 2; and D3, paragraphs [0018]-[0040]; figures 4, 7-9.

Therefore claim 30 lacks novelty in breach of **Article 33(2) PCT**. Moreover, the additional features introduced by dependent claims 31-34, 37-44 and 48-62 have also been anticipated by the same prior art. So this material is not new either.

- 2 Nor can the additional features of dependent claims 35, 36 and 45 provide any basis for new and inventive subject matter. This is because the fluorination treatment recommended in claims 35 and 36 is an obvious alternative to the measures adopted in the prior art for providing a hydrophobic surface, viz. self-assembling monolayers (SAMs), silanisation, or parylene coatings. Furthermore, it is entirely routine in the art to provide electrodes with hydrophilic, protective coatings. Therefore adopting these features, either singly or in combination, could never betoken inventive skill.

- 3 A method of using the apparatus for electrophysiological measurements in membrane protein analysis as set out in the independent method claim, claim 63, is contemplated in document **D1** and explicitly taught in documents **D2** and **D3**. So claim 63 lacks novelty as well.
- 4 Turning to the independent method claim, claim 1, which relates to a method for forming stable, high resistance lipid bilayer membranes, the International Searching Authority takes the view that this subject matter has been anticipated by the teaching of **D1** else is obvious, at the very least, in the light of document:

D4 = BIOPHYSICAL JOURNAL, vol. 86, no. 2, 1st February 2004, pages 955-965, XP002482463, ISSN 0006-3495; RÖMER W et al: "Impedance analysis and single-channel recordings on nano-black lipid membranes based on porous alumina"

(cf. D4, whole document). In view of **D1- D3**, the additional features recited in dependent claims 4-14, 17-29 can only be regarded as routine measures in this area of technology, which the skilled person would employ as a matter of course in implementing the teaching of claim 1. Consequently, this material must be deemed to lack inventive merit.

- 5 Nevertheless, there is nothing in the prior art cited pointing to the electrowetting step recited in dependent claim 3 by which the applicants adjust the amount of hydrophobic coating in the recess. This feature contributes materially to ensuring the reproducibility of the bilayer formation. Hence a method claim drafted to include this feature would apparently satisfy the requirements of **Article 33 PCT** in regard to novelty and inventive step.

INVENTION 2

- 1 The prior art document:

D5 = WO 97/16545 A1

discloses a device (20) for stimulating and measuring cell growth using electrically conducting polymers, and so an apparatus for conducting electro-physiological measurements (cf. D5, page 18, line 24 - page 21, line 12; examples 1-3; figures 3a, 3b). The device comprises:

- a body (22) having a recess in which an electrode (16) is located, wherein a conductive polymer is deposited on the electrode.

Therefore the subject matter of independent claim 68 is not new over this prior art, in contravention of **Article 33(2) PCT**. The same is true for dependent claims 69-71¹.

- 2 As noted above in section IV, the advantage conferred by claims 64-71 is to increase '... *the charge reservoir available to the electrodes...*' thereby stabilising the performance of the electrode and improving sensitivity. But it is already known from document:

D6 = WO 2007/028003 A2,

that '*... conducting polymer-based coatings are applied to electrodes... because the conducting polymer coatings provide enhanced electrode sensitivity and charge transfer capacity...*' in lab-on-a-chip devices (cf. D6, paragraphs [0111]-[0116]; [0143]-[0152] especially paragraphs [0116] and [0152]). Although there is no explicit disclosure of an electrode in recess, as set out in independent claim 64, the skilled person would regard it as entirely obvious to employ the teaching of **D6** in this situation too.

Therefore the International Searching Authority must conclude that claims 64-71 lack inventive merit over **D6**, in contravention of **Article 33(3) PCT**. Moreover, it would be particularly obvious to apply this teaching to the electrodes of the devices taught in document **D3**. Hence claims 46 and 47 are not inventive either in the light of this combination.

1. Claims 69-71 purport to be method claims dependent on apparatus claim 68. The International Searching Authority assumes this to be erroneous and only apparatus could have been intended.

- 3 On the face of it, claims 15 and 16 appear susceptible to a similar attack. However, documents **D1** and **D4**, employed against claim 1, do not apparently use metal electrodes. So there could never be any grounds for combining the teaching of these documents with **D6**. Consequently, it seems fair to conclude that claims 15 and 16 also satisfy the requirements of **Article 33 PCT** in regard to novelty and inventive step.
