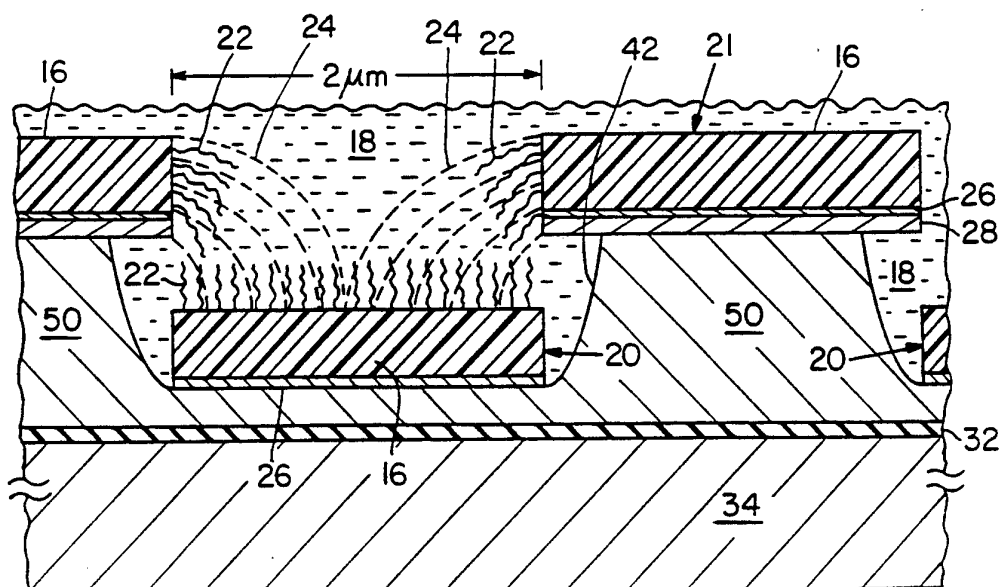




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification⁵ : G01N 33/543, C12Q 1/68 G01N 27/07, 21/75</p>	<p>A3</p>	<p>(11) International Publication Number: WO 93/22678 (43) International Publication Date: 11 November 1993 (11.11.93)</p>
<p>(21) International Application Number: PCT/US93/03829 (22) International Filing Date: 23 April 1993 (23.04.93) (30) Priority data: 07/872,582 23 April 1992 (23.04.92) US (71) Applicants: MASSACHUSETTS INSTITUTE OF TECHNOLOGY [US/US]; 77 Massachusetts Avenue, Cambridge, MA 02139 (US). BAYLOR COLLEGE OF MEDICINE [US/US]; 1 Baylor Plaza, Houston, TX 77030 (US). HOUSTON ADVANCED RESEARCH CENTER [US/US]; 4800 Research Forest Drive, The Woodlands, TX 77381 (US). (72) Inventors: HOLLIS, Mark, A. ; 45 Staffordshire Lane, Concord, MA 01742 (US). EHRlich, Daniel, J. ; 11 Grant Place, Lexington, MA 02173 (US). MURPHY, R., Allen ; 411 Hill Road, Boxboro, MA 01719 (US). KOSICKI, Bernard, B. ; 39 Fort Pont Road, Acton, MA 01720 (US). RATHMAN, Dennis, D. ; 42 East Bluff Road, Ashland, MA 01721 (US). CHEN, Chang-Lee ; 19 Pratts Mill Road, Sudbury, MA 01776 (US). MATHEWS, Richard, H. ; 30 Wildes Road, Chelmsford, MA 01824 (US). BURKE, Barry, E. ; 17 Sherburne Road, Lexington, MA 02173 (US). EGGERS, Mitch, D. ; 10 Plum Cove Court, The Woodlands, TX 77381 (US). HOGAN, Michael, E. ; 103 Golden Shadow Circle, The Woodlands, TX 77381 (US). VARMA, Rajender, Singh ; 8 Spurwood Court, The Woodlands, TX 77381-2526 (US).</p>	<p>(74) Agents: REYNOLDS, Leo, R. et al.; Hamilton, Brook, Smith & Reynolds, Two Militia Drive, Lexington, MA 02173 (US). (81) Designated States: CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 3 February 1994 (03.02.94)</p>	

(54) Title: OPTICAL AND ELECTRICAL METHODS AND APPARATUS FOR MOLECULE DETECTION



(57) Abstract

A method and apparatus are disclosed for identifying molecular structures within a sample substance using a monolithic array of test sites formed on a substrate upon which the sample substance is applied. Each test site includes probes formed therein to bond with a predetermined target molecular structure or structures. A signal is applied to the test sites and certain electrical, mechanical and/or optical properties of the test sites are detected to determine which probes have bonded to an associated target molecular structure.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 93/03829

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int. Cl. 5	G 01 N 33/543	C 12 Q 1/68
G 01 N 21/75		G 01 N 27/07
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int. Cl. 5	B 01 L	G 01 N C 12 Q
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ^o	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	WO, A, 9015070 (AFFYMAX TECHNOLOGIES NV) 13 December 1990 cited in the application see page 20, line 6 - page 22, line 24 see page 28, line 14 - line 36 see page 39, line 1 - page 40, line 28; claim 22 ---	1, 10, 50
X	EP, A, 0402917 (BIOCIRCUITS CORP) 19 December 1990 see column 3, line 57 - column 4, line 27 see column 7, line 7 - line 57 see column 9, line 58 - column 11, line 16 see column 16, line 56 - column 21, line 25; figures 1, 2 --- -/-	1, 10, 22 2
Y		
<p>^o Special categories of cited documents : ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
14-09-1993	29. 12. 93	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	<i>BINDON C.A.</i>	

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
Y	WO,A,9002327 (AUSTRALIAN MEMBRANE AND BIOTECHNOLOGY RESEARCH INSTITUTE) 8 March 1990 ---	2
A	WO,A,9002327 see page 25, line 13 - page 27, line 35; figures 8-10 ---	3-5
X	WO,A,9005300 (MIDWEST RESEARCH TECHNOLOGIES) 17 May 1990 see page 12, line 1 - page 18, line 8; figures 6-8 ---	1,10,22
A	EP,A,0347579 (MESSERSCHMITT-B\LKOW-BLOHM GMBH) 27 December 1989 see column 2, line 41 - column 4, line 26 see column 7, line 2 - column 9, line 44 ---	1,10,22
A	US,A,4963245 (WEETALL) 16 October 1990 see column 2, line 12 - column 3, line 13; figures ---	1-3,10,22
P,A	US,A,5187096 (GIAEVER ET AL.) 16 February 1993 see column 2, line 33 - column 5, line 63; figures 1,2 -----	1,2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 93/03829

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

For further information please see form PCT/ISA/206 mailed 27.09.93.

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-5, 10, 22, 50

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

US 9303829
SA 74062

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 16/12/93. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A- 9015070	13-12-90	US-A- 5143854	01-09-92
		AU-A- 5837190	07-01-91
		CA-A- 2054706	08-12-90
		EP-A- 0476014	25-03-92
		GB-A, B 2248840	22-04-92
		JP-T- 4505763	08-10-92
		NL-T- 9022056	02-03-92
EP-A- 0402917	19-12-90	US-A- 5156810	20-10-92
		CA-A- 2019039	15-12-90
		JP-A- 3128449	31-05-91
WO-A- 9002327	08-03-90	AU-A- 4078789	23-03-90
		EP-A- 0432188	19-06-91
		US-A- 5234566	10-08-93
WO-A- 9005300	17-05-90	AU-A- 4647589	28-05-90
		CA-A- 2002660	10-05-90
EP-A- 0347579	27-12-89	DE-A- 3818614	07-12-89
		DE-A- 3825907	01-02-90
		US-A- 5252294	12-10-93
		DE-U- 8817007	02-10-91
US-A- 4963245	16-10-90	US-A- 5066372	19-11-91
US-A- 5187096	16-02-93	None	

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82