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(21) International Application Number: PCT/US97/20195 (22) International Filing Date: 6 November 1997 (06.11.97) (30) Priority Data: 08/746,055 6 November 1996 (06.11.96) US 08/787,639 23 January 1997 (23.01.97) US 08/786,988 23 January 1997 (23.01.97) US 947,801 8 October 1997 (08.10.97) US (71) Applicant (for all designated States except US): SEQUENOM, INC. [US/US]; 11555 Sorrento Valley Road, San Diego, CA 92121 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): O'DONNELL, Maryanne, J. [US/US]; 3855 Nobel Drive, San Diego, CA 92122 (US). CANTOR, Charles, R. [US/US]; 11 Bay State Road, Boston, MA 02215 (US). LITTLE, Daniel, P. [US/US]; 393 Glendale Lake Road, Patton, PA 18668 (US). KOSTER, Hubert [DE/US]; 8636 C Via Mallorca Drive, La Jolla, CA 92037 (US). (74) Agent: SEIDMAN, Stephanie, L.; Brown Martin Haller & McClain, 1660 Union Street, San Diego, CA 92101-2926 (US).	(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). 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: 22 October 1998 (22.10.98)	
(54) Title: HIGH DENSITY IMMOBILIZATION OF NUCLEIC ACIDS		
(57) Abstract <p>Processes and kits for immobilizing a high density of nucleic acids on an insoluble surface, which are particularly useful for mass spectrometric detection of nucleic acids, are disclosed. Arrays containing the immobilized nucleic acids and use of the immobilized nucleic acids in a variety of solid phase nucleic acid chemistry applications, including nucleic acid synthesis (chemical and enzymatic), hybridization and/or extension, and sequencing, are provided. Serial and parallel dispensing tools that can deliver defined volumes of fluid to generate multi-element arrays of sample material on a substrate surface are further provided. Tools provided herein can include an assembly of vesicle elements, or pins, wherein each of the pins can include a narrow interior chamber suitable for holding nanoliter volumes of fluid. Methods for dispensing tools that can be employed to generate multi-element arrays of sample material on a substrate surface are also provided. The tool can dispense a spot of fluid to a substrate surface by spraying the fluid from the pin, contacting the substrate surface or forming a drop that touches against the substrate surface. The tool can form an array of sample material by dispensing sample material in a series of steps, while moving the pin to different locations above the substrate surface to form the sample array. The prepared sample arrays may be passed to a plate assembly that disposes the sample arrays for analysis by mass spectrometry.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/20195

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07H21/00 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07H C12Q B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 90 01564 A (MICROPROBE CORP) 22 February 1990	1-40
Y	see the whole document	1-40
A	see claims 1, 24, 46, 52, 68	107
X	US 5 547 835 A (KOSTER HUBERT) 20 August 1996	1, 5, 13, 20
Y	see column 10, line 1 - column 11, line 10 see column 13, line 15 - line 20 see example 1	1-40
A	see claim 1	107

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

<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 when the document is taken alone</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>
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Date of the actual completion of the international search 21 August 1998	Date of mailing of the international search report 03.09.98
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Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Scott, J
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INTERNATIONAL SEARCH REPORT

Int. l. Application No

PCT/US 97/20195

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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	see the whole document ---	1-40
X	DATABASE WPI Section Ch, Week 8844 Derwent Publications Ltd., London, GB; Class A96, AN 88-311964 XP002061833 & JP 63 230 086 A (NITTO ELECTRIC IND CO) , 26 September 1988	1,3
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Y	WO 93 09668 A (AFFYMAX TECH NV) 27 May 1993	1-40
A	see the whole document	83,113, 118
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Y	WO 89 12624 A (CETUS CORP) 28 December 1989 see the whole document ---	1-40
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A	see page 12 - page 13	41,65
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 457 041 A (GINAVEN ROBERT O ET AL) 10 October 1995 see abstract ---	41,65
A	EP 0 339 781 A (BECKMAN INSTRUMENTS INC) 2 November 1989 see abstract ---	41,65
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A	US 5 312 233 A (TANNY MARK N ET AL) 17 May 1994 see abstract ---	41,65
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INTERNATIONAL SEARCH REPORT

International application No.

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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:

See further information sheet

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.:

Remark on Protest

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-40

A method of immobilizing a nucleic acid on a solid support; an insoluble support with the nucleic acid covalently bound to it; a kit for immobilizing the nucleic acid; a method for forming an array of nucleic acids on a substrate surface.

2. Claims: 41-64

A device for dispensing nanovolumes of fluid in chemical or biological procedures onto the surface of a substrate.

3. Claims: 65-82

A fluid dispensing device for dispensing a fluid in chemical or biological procedures into one or more wells of a multi-well substrate.

4. Claims: 83-106

A method for forming an array of sample material on the surface of a substrate according to the procedure of claim 83.

5. Claims: 107-112

A method for analyzing a material according to the procedure of claim 107.

6. Claims: 113-117

An apparatus for forming an array of a sample material on the surface of a substrate according to the procedure of claim 113.

7. Claims: 118-121

A substrate having a surface carrying an array of matrix material according to claim 118.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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