



US005547839A

United States Patent

[19]

Dower et al.**Patent Number:** 5,547,839**Date of Patent:** Aug. 20, 1996**[54] SEQUENCING OF SURFACE IMMOBILIZED POLYMERS UTILIZING MICROFLOURESCENCE DETECTION****[75] Inventors:** William J. Dower, Menlo Park; Stephen P. A. Fodor, Palo Alto, both of Calif.**[73] Assignee:** Affymax Technologies N.V., Curacao, Netherlands Antilles**[21] Appl. No.:** 626,730**[22] Filed:** Dec. 6, 1990**Related U.S. Application Data****[63]** Continuation-in-part of Ser. No. 492,462, Mar. 7, 1990, Pat. No. 5,143,854, which is a continuation-in-part of Ser. No. 362,901, Jun. 7, 1989, abandoned.**[51] Int. Cl.⁶** C12Q 1/68**[52] U.S. Cl.** 435/6; 536/24.33; 536/24.3**[58] Field of Search** 435/6, 91, 810, 435/973, 975, 91.2; 436/527, 530, 531, 56, 94, 800, 808; 536/27, 24.33; 935/77**[56] References Cited****U.S. PATENT DOCUMENTS**

4,542,102	9/1985	Dattagupta et al. 435/6
4,582,789	4/1986	Sheldon et al. 435/6
4,656,127	4/1987	Mundy 435/6
4,689,405	8/1987	Frank et al. 536/27
4,713,326	12/1987	Dattagupta et al. 435/6
4,855,225	8/1989	Fung et al. 435/6
4,889,818	12/1989	Gelfand et al. 435/194
4,962,037	10/1990	Jett et al. 435/6
4,965,188	10/1990	Mullis et al. 435/6
5,002,867	3/1991	Macevicz 435/6
5,026,840	6/1991	Dattagupta et al. 536/27
5,075,216	12/1991	Innis et al. 435/6
5,126,239	6/1992	Livak et al. 435/6
5,143,854	9/1992	Pirrung et al. 436/518

FOREIGN PATENT DOCUMENTS

392546	10/1990	European Pat. Off.
2233654	1/1991	United Kingdom .

9013666 5/1990 WIPO C12Q 1/68
 9015070 12/1990 WIPO .
 9107087 5/1991 WIPO .
 9106678 5/1991 WIPO C12Q 1/68

OTHER PUBLICATIONS

Ikehara et al., "The Synthesis of Polynucleotides," *Advances in Carbohydrate Chemistry and Biochemistry* (1979) 36:135-213.

Tsugita et al., "Sensitization of Edman Amino Acid Derivatives Using the Fluorescent Reagent, 4-Aminofluorescein," *J. Biochem.* (1989) 106:60-65.

Ross et al., "Interstrand Crosslinks due to 4,5',8-Trimethyl-psoralen and Near Ultraviolet Light in Specific Sequences of Animal DNA," *J. Mol. Biol.* (1988) 201:339-351.

Barinaga, 27 Sep. 1991, *Science* 253:1489.

Fodor et al., 15 Feb. 1991, *Science* 251:767-773.

Dower and Fodor, 1991, *Ann. Rep. Med. Chem.* 26:271-280.

Little, 16 Aug. 1990, *Nature* 346:611-612.

Craig et al., 1990, *Nucl. Acids. Res.* 18:2653-2660.

Chatterjee et al., 1990, *J. Am. Chem. Soc.* 112:6397-6399.

Pfeifer et al., 10 Nov. 1989, *Science* 246:810-812.

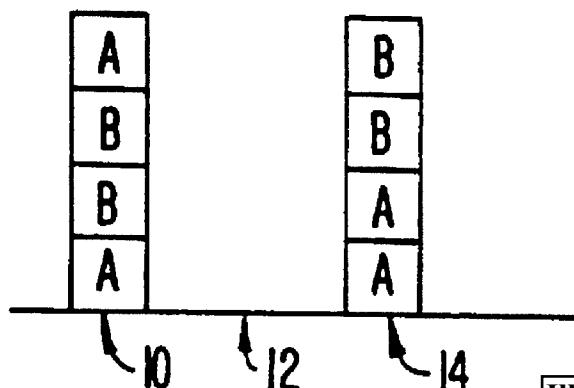
Evans et al., Jul. 1989, *Proc. Natl. Acad. Sci. USA* 86:5030-4.

Saiki and Gelfand, 1989, *Amplifications* 1:4-6.

(List continued on next page.)

Primary Examiner—W. Gary Jones**Assistant Examiner**—Scott Houtteman**Attorney, Agent, or Firm**—Townsend & Townsend & Crew LLP**[57] ABSTRACT**

Means for simultaneous parallel sequence analysis of a large number of biological polymer macromolecules. Apparatus and methods may use fluorescent labels in repetitive chemistry to determine terminal monomers on solid phase immobilized polymers. Reagents which specifically recognize terminal monomers are used to label polymers at defined positions on a solid substrate.

7 Claims, 10 Drawing Sheets

Illumina Ex. 1030

IPR Petition - USP 10,435,742

OTHER PUBLICATIONS

- Nelson et al., 1989, Nuc. Acids Res. 17(18):7179–7186.
McCray et al., 1989, Ann. Rev. Biophys. Biophys. Chem. 18:239–270.
Knight, 1989, Bio/Tech. 7:1075–1076.
Carrano et al., 1989, Genomics 4:129–136.
Innis et al., Dec. 1988, Proc. Natl. Acad. Sci. USA 85:9436–9440.
Frank et al., Oct. 1988 Bio/Tech. 6:1211–1213.
Kambara et al., Jul. 1988, Bio/Tech. 6:816–821.
Bains et al., 1988, J. Theor. Biol. 135:303–307.
Ye and Hong, May 1987, Scientia Sinica 30(5):503–506.
Tabor and Richardson, Jul. 1987, Proc. Natl. Acad. Sci. USA 84:4767–4771.
Tabor and Richardson, 15 Nov. 1987, J. Biol. Chem. 262:15330–15333.
Prober et al., 1987, Science 238:336–341.
Michiels et al., 1987, CABIOS 3(3):203–210.
Coulson et al., Oct. 1986, Proc. Natl. Acad. Sci. USA 83:7821–5.
Olson et al., Oct. 1986, Proc. Natl. Acad. Sci. USA 83:7826–7830.
Smith et al., 12 Jun. 1986, Nature 321:674–679.
Poustka et al., 1986, CSH Symp. Quant. Biol. 51:131–139.
Kutateladze et al., 1986, Molekulyarnaya Biologiya 20:267–276 (abstract only).
Gerard et al., DNA 5(4):271–279.
Wood et al., Mar. 1985, Proc. Natl. Acad. Sci. USA 82:1585–1588.
Smith et al., 1985, Nuc. Acids Res. 13(7):2399:2412.
Kotewicz et al., 1985, Gene 85:249–258.
Cimino et al., 1985, Ann. Rev. Biochem. 54:1151–1193.
Chidgeavadze et al., Apr. 1985, FEBS Lett. 183(2):275–278.
Chidgeavadze et al., 1984, Nuc. Acids Res. 12(3):1671–1686.
Seed, 1982, Nuc. Acids Res. 10(5):1799–1810.
Ruth et al., 1981, Mol. Pharm. 20:415–422.
Maxam and Gilbert, 1980, Meth. Enz. 65:499–560.
Parsons, 1980, Photochem. Photobiol. 32:813–821.
Song et al., 1979, Photochem. Photobiol. 29:1177–1197.
Houts, Feb. 1979, J. Virol. 29:517–522.
Wiesehahn et al., Jun. 1978, Proc. Natl. Acad. Sci. USA 75:2703–2707.
Sanger et al., Dec. 1977, Proc. Natl. Acad. Sci. USA 74(12):5463–5467.
Chien et al., 1976, J. Bacteriol. 127:1550–1557.
Sanger and Coulson, 1975, J. Mol. Biol. 94:441–448.
Ohtsuka et al., 1974, Nuc. Acids Res. 1(10):1351–1357.
Nossal, 1974, J. Biol. Chem. 249(17):5668–5676.
Jacobsen et al., 1974, Eur. J. Biochem. 45:623–627.
Amit et al., 1974, J. Org. Chem. 39(2):192–196.
Patchornik et al., 21 Oct. 1970, J. Am. Chem. Soc. 92(21):6333–6335.
Klenow and Henningsen, Jan. 1970, Proc. Natl. Acad. Sci. USA 65(2):168–175.

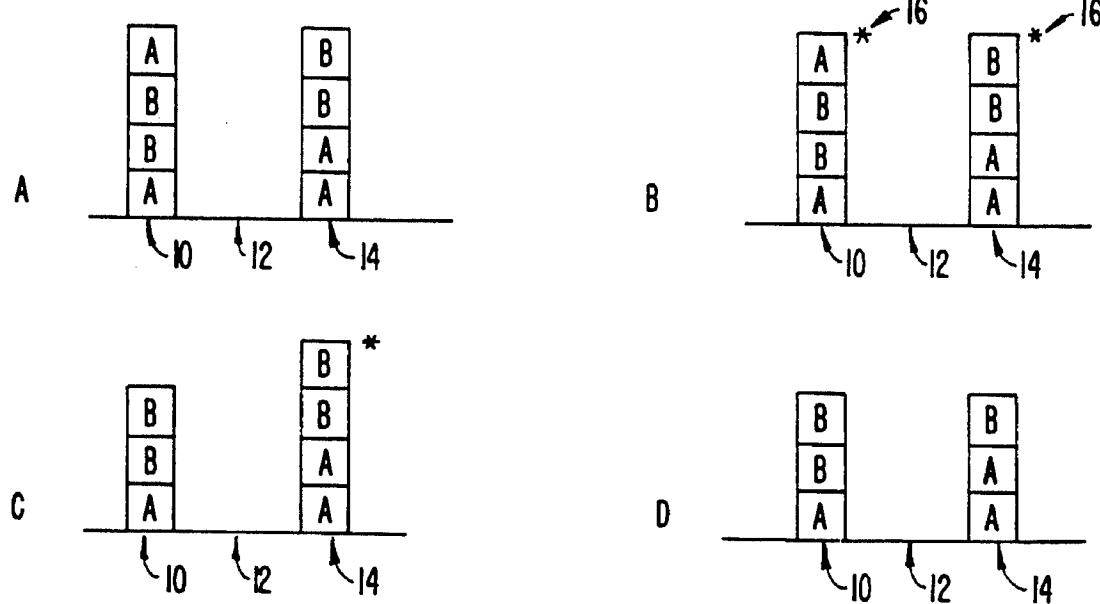


FIG. 1.

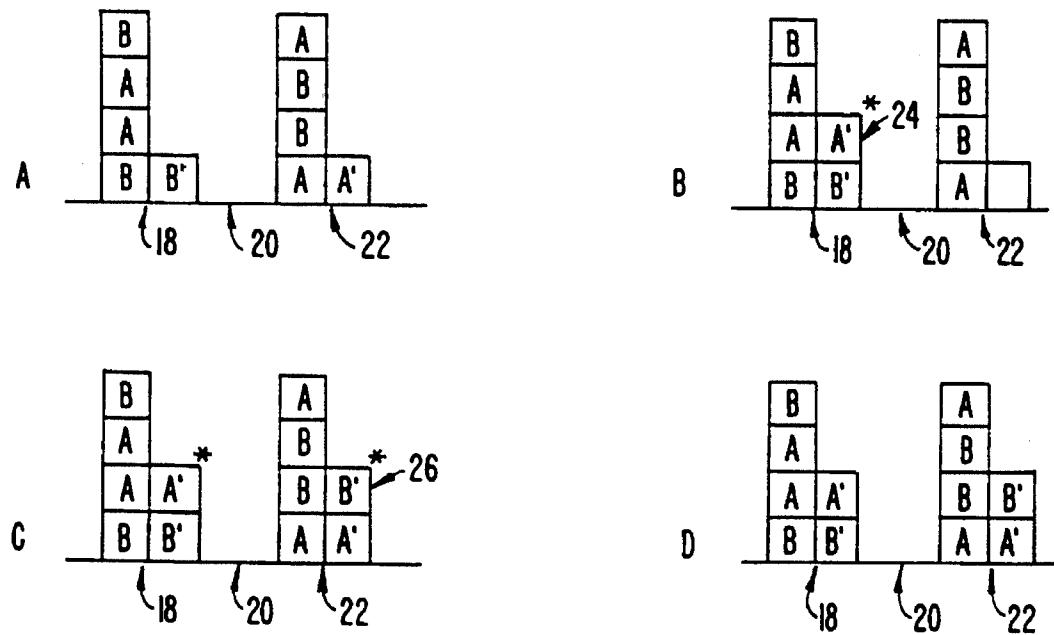
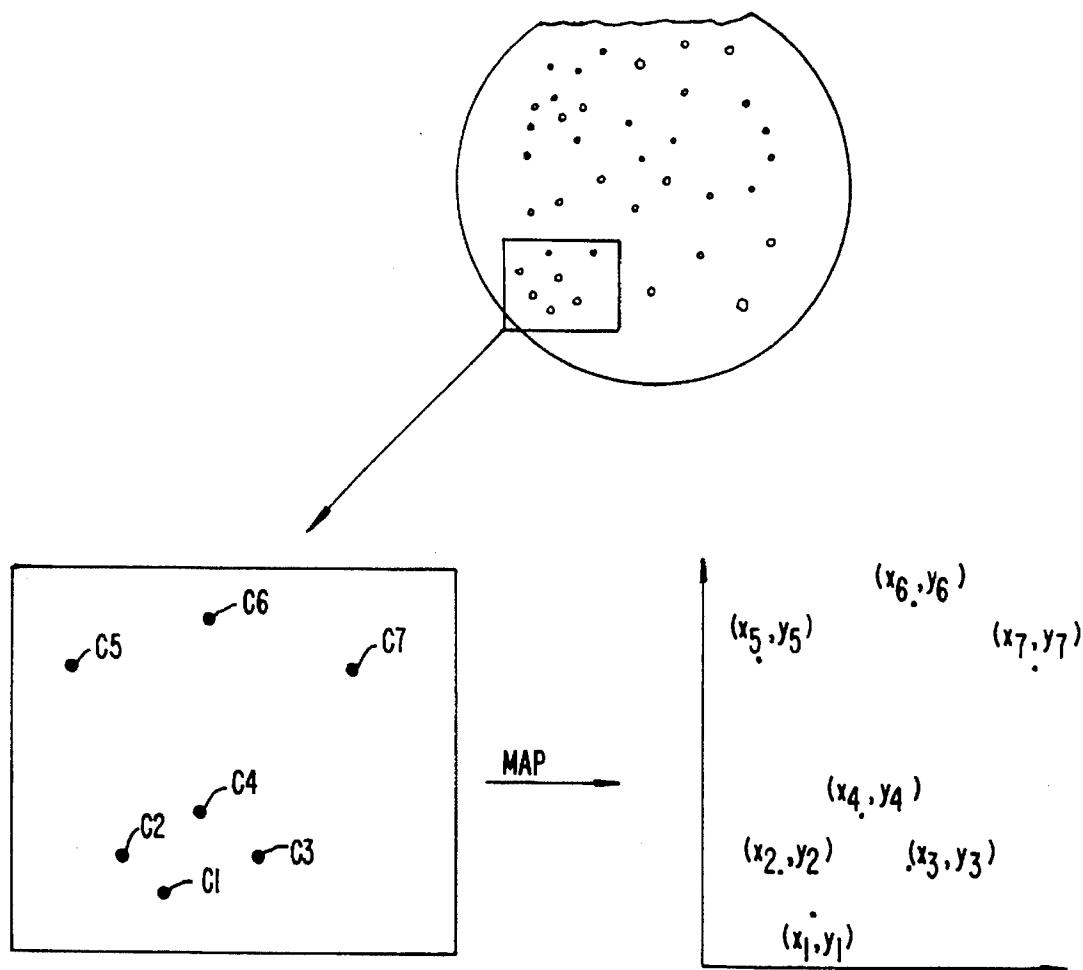


FIG. 2.



CLUSTERS LOCALIZED AT POSITIONS

C_1	(x_1, y_1)
C_2	(x_2, y_2)
C_3	(x_3, y_3)
C_4	(x_4, y_4)
C_5	(x_5, y_5)
C_6	(x_6, y_6)
C_7	(x_7, y_7)
:	:
C_n	(x_n, y_n)

FIG. 3.

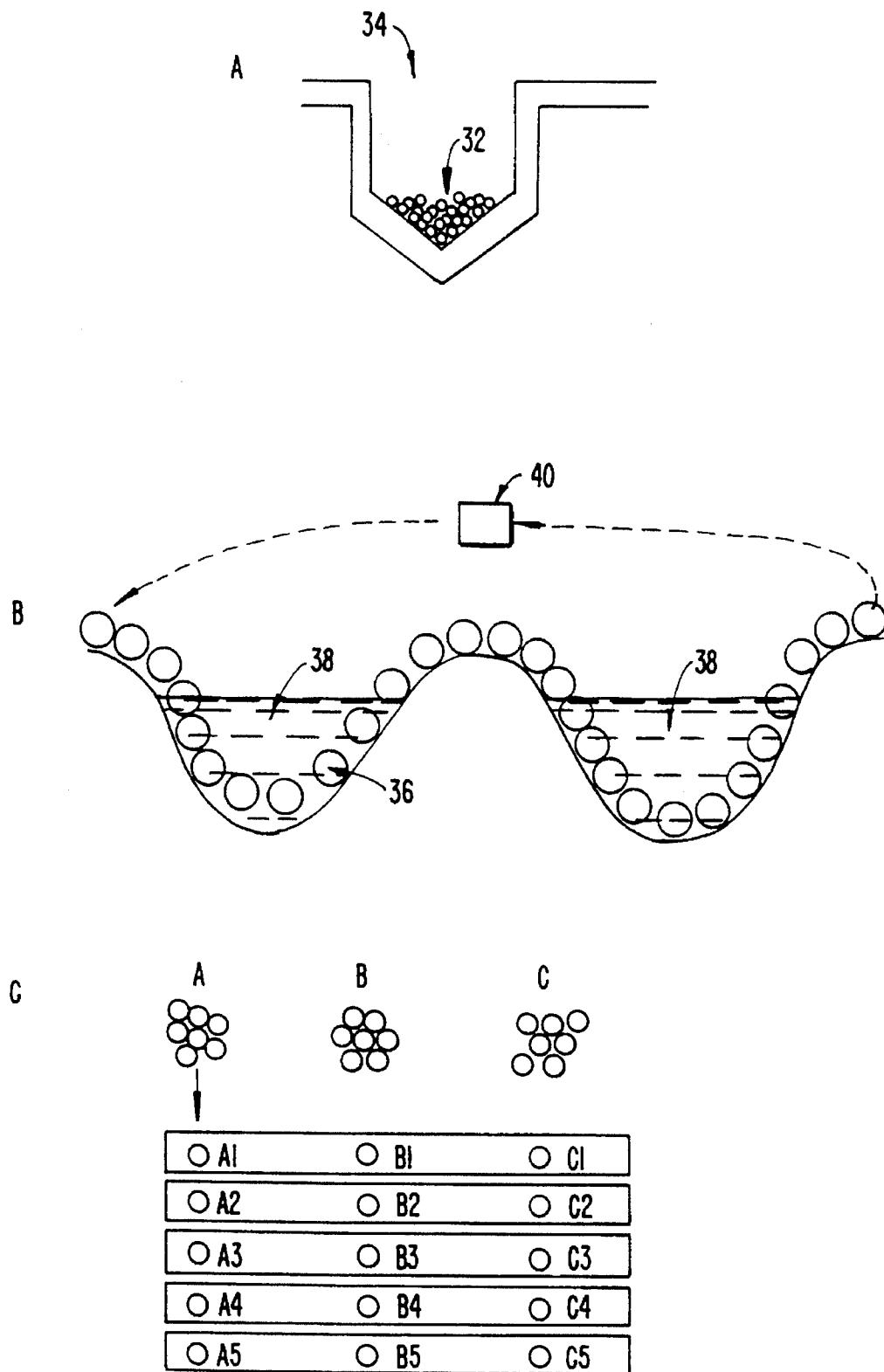


FIG. 4.

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