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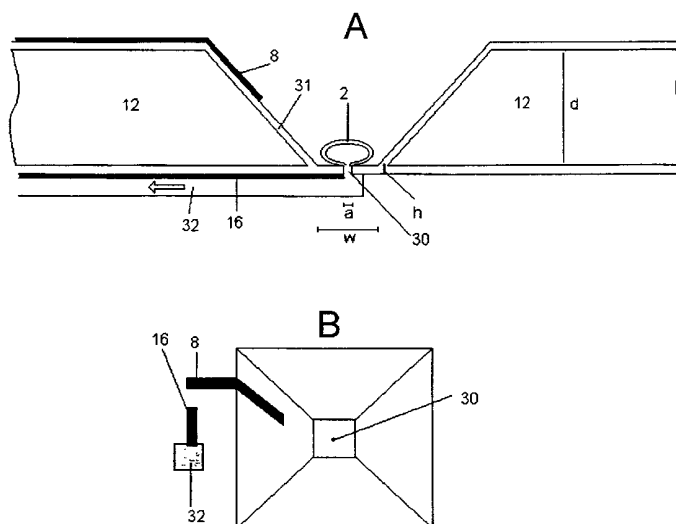
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(54) Title: A SUBSTRATE AND A METHOD FOR DETERMINING AND/OR MONITORING ELECTROPHYSIOLOGICAL PROPERTIES OF ION CHANNELS



(57) Abstract: The present invention relates to a substrate and a method for obtaining an electrophysiological measuring configuration in which a cell forms a high resistive seal (giga-seal) around a measuring electrode making it suitable for determining and monitoring a current flow through the cell membrane. The substrate is typically part of an apparatus for studying electrical events in cell membranes, such as an apparatus for carrying out patch clamp techniques utilised to study ion transfer channels in biological membranes. The substrate has a plurality or an array of measuring sites with integrated measuring and reference electrodes formed by wafer processing technology. The electrodes are adapted to conduct a current between them by delivery of ions by one electrode and receipt of ions by the other electrode and are typically silver/silver halide electrodes. This allows for effective and fast measuring of cells in configurations where there is a direct electrical connection between the measuring electrode and the cell interior, a whole-cell measuring configuration.



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INTERNATIONAL SEARCH REPORT

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

B. FIELDS SEARCHED

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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)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 299 778 A (STANFORD RES INST INT) 18 January 1989 (1989-01-18) page 3; figure 11 ---	1-28
X	US 4 225 410 A (PACE SALVATORE J) 30 September 1980 (1980-09-30) abstract; figures 6,8 ---	1-15
X	US 4 062 750 A (BUTLER JAMES FRANCIS) 13 December 1977 (1977-12-13) abstract; figure 4 ---	1-15
X	EP 0 299 779 A (STANFORD RES INST INT) 18 January 1989 (1989-01-18) figure 3 ---	1-15
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Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

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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	M. MULLENBORN ET AL: "Fast 3d Laser Micromachining of Silicon for Micromechanical and Microfluid Applications" , SOLID-STATE SENSORS AND ACTUATORS, 1995 AND EUROSensors IX.. TRANSDUCERS '95. THE 8TH INTERNATIONAL CONFERENCE ON, , STOCKHOLM, SE XP002901487 page 166 -page 169; figure 7 ---	1-28
P,A	WEAVER J C: "Electroporation of cells and tissues " IEEE TRANSACTIONS ON PLASMA SCIENCE, vol. 28, no. 1, February 2000 (2000-02), pages 24-33, XP002901488 abstract -----	24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT, No. 00/00548

Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date
EP 0299778	A	18-01-1989	US 4874500 A CA 1298873 A JP 1112149 A	17-10-1989 14-04-1992 28-04-1989

US 4225410	A	30-09-1980	CA 1136701 A DE 2963565 D EP 0012035 A	30-11-1982 14-10-1982 11-06-1980

US 4062750	A	13-12-1977	NONE	

EP 0299779	A	18-01-1989	US 4812221 A AT 124140 T CA 1291208 A DE 3854021 D DE 3854021 T JP 1088245 A JP 2070765 C JP 7104322 B	14-03-1989 15-07-1995 22-10-1991 27-07-1995 02-11-1995 03-04-1989 10-07-1996 13-11-1995
