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61/042,116 3 April 2008 (03.04.2008) US(71) Applicant (for all designated States except US): **Yissum, Research Development Company of the Hebrew University of Jerusalem** [IL/IL]; Hi Tech Park, The Edmond J. Safra Campus., The Hebrew University of Jerusalem, 91390 Jerusalem (IL).

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[Continued on next page]

(54) Title: METHOD AND APPARATUS FOR MONITORING PROCESSES IN LIVING CELLS

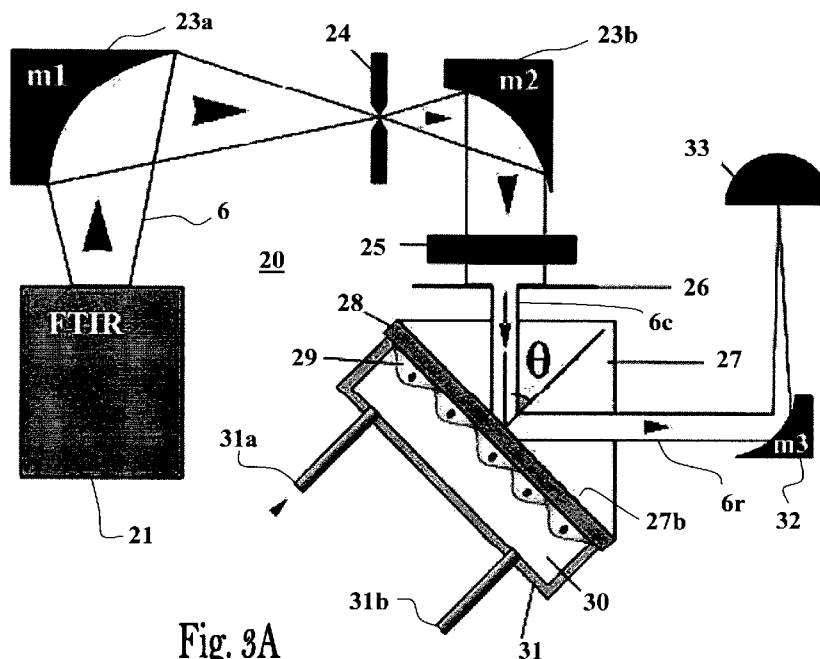


Fig. 3A

(57) Abstract: The invention provides a method and apparatus for monitoring processes in living cells by measuring optical reflectivity by Surface Plasmon Resonance at the surface and/or inside living cells attached to a thin metal film (28), wherein said thin metal film is attached or optically coupled to a base of a prism (27) such that a collimated and optically polarized light beam (6c) in the near-infrared and/or mid-infrared wavelength ranges directed to a side surface of the prism is internally reflected by said prism at its base (27b) and measured by detector means (33) capable of measuring the intensity and optionally also polarization or phase of the reflected beam (6r).

**Published:****(88) Date of publication of the international search report:**

1 October 2009

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2008/001671

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N21/55 G01N21/35

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)

G01N

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, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 330 062 B1 (CORN ROBERT M [US] ET AL) 11 December 2001 (2001-12-11) * abstract; col. 1, lines 21-39; col. 3, line 64 to col. 5, line 27; figures 1,2*	1, 2, 33, 34
P, X	LE PERSON ET AL: "Surface plasmon resonance in chalcogenide glass-based optical system" SENSORS AND ACTUATORS B, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 130, no. 2, 26 December 2007 (2007-12-26), pages 771-776, XP022550398 ISSN: 0925-4005 the whole document ----- -/--	1, 2, 33, 34

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *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)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *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
- *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
- *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.
- *G* document member of the same patent family

Date of the actual completion of the international search

29 April 2009

Date of mailing of the international search report

10/08/2009

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2008/001671

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	LIRTSMAN V ET AL: "Infrared surface plasmon resonance technique for biological studies" JOURNAL OF APPLIED PHYSICS, AMERICAN INSTITUTE OF PHYSICS. NEW YORK, US, vol. 103, no. 1, 11 January 2008 (2008-01-11), pages 14702-14702, XP012108661 ISSN: 0021-8979 the whole document	1,2,33, 34
P,X	SYLVAIN HERMINJARD ET AL: "Surface plasmon resonance spectroscopy in the mid-infrared range" LASERS AND ELECTRO-OPTICS, 2008. CLEO 2008. CONFERENCE ON, IEEE, PISCATAWAY, NJ, USA, 4 May 2008 (2008-05-04), pages 1-2, XP031277247 ISBN: 978-1-55752-859-9 the whole document	1,2,33, 34
A	BRINK G ET AL: "Near-infrared surface plasmon resonance in silicon-based sensor: new opportunities in sensitive detection of biomolecules from aqueous solutions by applying microstep for discriminating specific and non-specific binding" SENSORS AND ACTUATORS B, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 25, no. 1-3, 1 April 1995 (1995-04-01), pages 756-761, XP004309330 ISSN: 0925-4005 * section "1. Introduction" *	1,33
A	PATSKOVSKY S ET AL: "Properties and sensing characteristics of surface-plasmon resonance in infrared light" JOURNAL OF THE OPTICAL SOCIETY OF AMERICA A, OPTICAL SOCIETY OF AMERICA, US, vol. 20, no. 8, 1 August 2003 (2003-08-01), pages 1644-1650, XP007908292 ISSN: 1084-7529 * section "1. Introduction" *	1,33
A	WO 2004/029582 A (UNIV NORTH CAROLINA [US]; FRANZEN STEFAN [US]; BREWER SCOTT [US]) 8 April 2004 (2004-04-08) * page 9, lines 8-31; page 13, line 30 to page 14, line 17; figure 5A *	1,33
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2008/001671

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>JAY VIZGAITIS: "Selecting Infrared Optical Materials" INTERNET CITATION, [Online] 14 December 2006 (2006-12-14), XP007908301 Retrieved from the Internet: URL:www.optics.arizona.edu/optomech/studen t%20reports/tutorials/2006/VizgaitisTutori all.doc> [retrieved on 2009-04-22] the whole document</p> <p>-----</p>	1,33

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2008/001671

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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 No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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, 2, 33, 34

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ 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: 1,2,33,34

Prism geometry and orientation in a surface plasmon
resonance system

2. claims: 3,15,16,37

A light delivery system and the orientation of a prism
relative to the light delivery system

3. claims: 4,7,8,36

Plural probe regions and corresponding beam processing means

4. claims: 5,6

A cuvette

5. claims: 9,13

Particular features of a metal film on the prism

6. claim: 10

A prism material

7. claims: 11, 12, 17-32 and 40-46

A replaceable surface and the surface plasmon resonance
measurement configuration

8. claims: 14,35

A light source

9. claims: 38,39

A measurement method including external stimuli

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2008/001671

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6330062	B1	11-12-2001	NONE
WO 2004029582	A	08-04-2004	AU 2003278993 A1
			19-04-2004