(51) International Patent Classification 7: G01N 33/53

(21) International Application Number: PCT/US2002/022681

(22) International Filing Date: 17 July 2002 (17.07.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
- 60/347,821 23 October 2001 (23.10.2001) US
- 60/354,668 6 February 2002 (06.02.2002) US


(74) Agent: ANTLER, Adrienne M.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).


Published:
- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report: 11 May 2006

For two-letter codes and other abbreviations, refer to the “Guidance Notes on Codes and Abbreviations” appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD AND APPARATUS USING A NONLINEAR OPTICAL TECHNIQUE FOR DETECTION OF PROBE-TARGET INTERACTIONS IN A FIELD

(57) Abstract: A nonlinear optical technique, such as second or third harmonic or sum or difference frequency generation, is used to detect binding interactions, or the degree or extent of binding, in an applied external force field. The external field is used to create non-centrosymmetric region in a sample comprising the probes and/or targets. Targets and probes can be labeled with nonlinear-active moieties, or modulators of the nonlinear active properties of these moieties. In one aspect of the present invention, the nonlinear optical technique detects a change in nonlinear activity in an applied external force field of a probe due to target binding. In another aspect of the invention, the nonlinear optical technique screens candidate probes by detecting a change in nonlinear activity in an applied external force field due to a probe-target interaction. In another aspect of the invention, the nonlinear optical technique screens candidate modulators of a probe-target interaction by detecting a change in nonlinear activity in an applied external force field in the presence of the modulator.
INTERNATIONAL SEARCH REPORT

International application No. PCT/US02/22681

A. CLASSIFICATION OF SUBJECT MATTER
   IPC(7)  : G01N 33/53
   US CL.  : 455/7.1
   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)
   U.S. : 435/7.1

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

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>US 6,096,497 (Bauer et al.) 1 Aug 2000 (01.08.2000) Col. 6, line 33-53, Background</td>
<td>141-174</td>
</tr>
</tbody>
</table>

מינים documentos listados en la continuidad de la caja C. See patent family annex.

Date of the actual completion of the international search: 13 January 2006 (13.01.2006)

Date of mailing of the international search report: 23 MAR 2006

Name and mailing address of the ISA/US
   Mail Stop PCT, Attn: ISA/US
   Commissioner of Patents
   P.O. Box 1450
   Alexandria, Virginia 22313-1450

Authorized officer
   Jacob Cheu
   Telephone No. 571-272-0814

Faximile No. (571) 273-3201

Form PCT/ISA/210 (second sheet) (July 1998)
### DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>