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(54) **Title:** METHOD AND APPARATUS FOR HIGH THROUGHPUT DIAGNOSIS OF DISEASED CELLS WITH MICROCHANNEL DEVICES

(57) **Abstract:** The method and apparatus of the present invention detects changes in cell biomechanics caused by any of a variety of diseases and conditions. In one embodiment, the method and apparatus of the invention detect infection of red blood cells. In one embodiment, the invention is a method and apparatus comprising a microfluidic channel with a constriction, for trapping infected red blood cells while allowing healthy red blood cells to deform and pass through the channel. In another embodiment, the invention comprises a suspended microchannel resonator for detecting and counting red blood cells at the constriction of the microfluidic channel.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/00442

A. CLASSIFICATION OF SUBJECT MATTER IPC: GOIN 33/49(2006.01) USPC: 435/287.1 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. : 435/287.1 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 practicable, search terms used) EAST (search term: microchanne!)														
C. DOCUMENTS CONSIDERED TO BE RELEVANT														
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.												
Y	US 2005/0064581 A1 (MANALIS et al) 24 March 2005 (24.03.2005), page 4, paragraph 0036, page 6, paragraph 0060, page 7, paragraph 0067, FIGs. 1 and 11, claim 1.	1-47, 54-56												
Y	US 2004/0168982 A1 (BITENSKY et al) 02 September 2004 (02.09.2004), page 2, paragraph 0017, 0014, page 3, paragraph 0026, 0030, FIGs. 1-3.	1-47, 54-56												
A	US 2002/0142285 A1 (BITENSKY et al) 03 October 2002 (03.10.2002) see the whole documents	1-47 and 54-56												
<input type="checkbox"/> I Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.														
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;">* Special categories of cited documents</td> <td style="width: 50%; border: none;">"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</td> </tr> <tr> <td style="border: none;">"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td style="border: none;">"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</td> </tr> <tr> <td style="border: none;">"E" earlier application or patent published on or after the international filing date</td> <td style="border: none;">"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</td> </tr> <tr> <td style="border: none;">"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)</td> <td style="border: none;">"&" document member of the same patent family</td> </tr> <tr> <td style="border: none;">"O" document referring to an oral disclosure, use, exhibition or other means</td> <td style="border: none;"></td> </tr> <tr> <td style="border: none;">"P" document published prior to the international filing date but later than the priority date claimed</td> <td style="border: none;"></td> </tr> </table>			* Special categories of cited documents	"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	"A" document defining the general state of the art which is not considered to be of particular relevance	"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	"E" earlier application or patent published on or after the international filing date	"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	"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)	"&" document member of the same patent family	"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	
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"P" document published prior to the international filing date but later than the priority date claimed														
Date of the actual completion of the international search 14 November 2007 (15.11.2007)		Date of mailing of the international search report 16 JUN 2008												
Name and mailing address of the ISA/US Mail Stop PCT, Ann ISA/US Commissioner for Patents P O Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer <i>David Fox</i> DAVID FOX Telephone No. 571-272-1600												

Box No. H 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:

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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. **D** 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:
Please See Continuation 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 additional fees, this Authority did not invite payment of any additional fees.
 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.. 1-47 and 54-56
 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 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.

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-15, drawn to a method for detecting an abnormality in a cell, comprising introducing the cell into a suspended microchannel resonator, and detecting the cell within the microchannel, wherein the microchannel resonator comprises a constriction.

Group II, claims 16-47, and 54-56, drawn to an apparatus comprising a microchannel resonator.

Group III, claims 48-51, drawn to a method for detecting or monitoring a disease or clinical condition in a subject, comprising providing a sample containing cells obtained from the subject, flowing the cells through a microchannel, and detecting cells in the microchannel.

Group IV, claims 52-53, drawn to a method of detecting or monitoring a disease or clinical condition in a subject, comprising providing a sample, and detecting an abnormality in the stiffness of the cells.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The method of Group I lacks unity of invention with Groups III, IV and the apparatus of Group II. The method of Group I requires introducing cells into a microchannel and detecting the cells. This is not a special technical feature which is shared by the other. Bitensky et al (US2004/0168982 A1) disclose a method which requires introducing cells into a microchannel and detecting the cells (see page 5, claim 22). The method of Group III, IV and the apparatus of Group II are not limited in scope as to require the method of Group I. So therefore Group I-IV lack a special technical feature.