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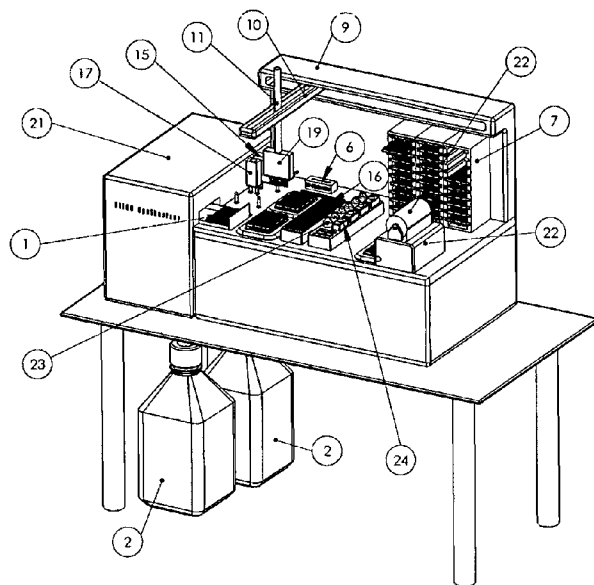
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(54) Title: INTEGRATED INSTRUMENT PERFORMING SYNTHESIS AND AMPLIFICATION

Fig. 1



(57) Abstract: The present invention is directed to an integrated system for oligonucleotide synthesis and PCR. The integrated instrument of the inventive system is basically composed of two independent modules which are operatively linked to each other. The first module is a unit for the chemical de novo synthesis of oligonucleotides such as oligonucleotide primers and/or oligonucleotide hybridization probes. The second module is a unit for performing an analytical polymerase chain reaction amplification in real time, i.e. a qPCR. The two modules are operatively linked to each other in such a way that a user can load a nucleic sample that shall be analyzed into the inventive instrument and perform a PCR reaction by programming the instrument without a previous external synthesis of oligonucleotide amplification primers.



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<b>B. FIELDS SEARCHED</b>		
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<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/086829 A1 (LIVESAY ERIC A [US] ET AL) 8 May 2003 (2003-05-08) cited in the application paragraph [0066] paragraph [0101] - paragraph [0103]	1-10
Y	US 2002/176811 A1 (PECK KONAN [TW] ET AL) 28 November 2002 (2002-11-28) cited in the application paragraph [0045]	1-10
Y	US 2008/003649 A1 (MALTEZOS GEORGE [US] ET AL) 3 January 2008 (2008-01-03) the whole document	1-10
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
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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.
Y	US 6 174 670 B1 (WITTWER CARL T [US] ET AL) 16 January 2001 (2001-01-16) cited in the application column 26, line 40 - line 42 -----	1-10
A	DE 297 20 432 U1 (MWG BIOTECH GMBH [DE]; HEIMBERG WOLFGANG DR [DE]) 25 March 1999 (1999-03-25) * Figure * -----	1-10

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No  
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Patent document cited in search report	A1	Publication date	Patent family member(s)	Publication date
US 2003086829	A1	08-05-2003	NONE	
US 2002176811	A1	28-11-2002	NONE	
US 2008003649	A1	03-01-2008	NONE	
US 6174670	B1	16-01-2001	AT 295427 T	15-05-2005
			AT 428801 T	15-05-2009
			AT 318327 T	15-03-2006
			AU 726501 B2	09-11-2000
			AU 3481297 A	05-01-1998
			CA 2257109 A1	11-12-1997
			CA 2658290 A1	11-12-1997
			DE 69733282 D1	16-06-2005
			DE 69733282 T2	19-01-2006
			DE 69735313 T2	02-11-2006
			EP 0912766 A1	06-05-1999
			ES 2243393 T3	01-12-2005
			JP 2000509608 T	02-08-2000
			JP 4118932 B2	16-07-2008
			JP 2007185188 A	26-07-2007
			JP 2008173127 A	31-07-2008
			NZ 333136 A	27-03-2000
			PT 1179600 E	31-08-2005
			WO 9746714 A1	11-12-1997
DE 29720432	U1	25-03-1999	AT 201101 T	15-05-2001
			WO 9926070 A2	27-05-1999
			EP 1032839 A2	06-09-2000
			JP 4272351 B2	03-06-2009
			JP 2001523823 T	27-11-2001
			US 6656724 B1	02-12-2003