(51) International Patent Classification:
G01N 15/14 (2006.01)

(21) International Application Number:
PCT/IE2006/000047

(22) International Filing Date: 5 May 2006 (05.05.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
S2005/0304 11 May 2005 (11.05.2005) IE

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(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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(54) Title: A MOBILE CHEMISTRY AND HAEMATOLOGY ANALYSER WITH AN INTEGRATED DIAGNOSTIC DATABASE

(57) Abstract: A portable biological fluid testing system comprising at least one sensor cartridge (3) having at least one sensor, an analyser (1) adapted to analyse readings from said at least one sensor, said analyser (1) comprising means for calculating cell count and means for calculating at least one analyte measurement, and a data processor (2) for processing said results, said data processor (2) comprising an interactive database.
Published:
— with international search report

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.
Title
A mobile chemistry and haematology analyser with an integrated diagnostic databank.

Field of the Invention
The present invention relates to blood analysis. In particular, the invention relates to a portable system for rapidly analysing small volumes of a fluid sample, such as blood.

Background to the Invention
Blood analysis today is predominantly the realm of large central laboratories. For years the trend has been towards centralisation, however this often results in longer waits and a higher risk of error due to the increased number of steps which require some kind of human intervention. These include sample transport, sample preparation, sample storage, sample labeling, data recording, data reporting, data interpretation not to mention that often different labs within a central facility perform different tests therefore this increases the error potential through sample splitting, and reintegration of result/data.

Gascoyne and Vykoukal 2004 (Proceedings of the IEEE, Vol. 92, No. 1) report that 90% of the cost and 95% of the time to obtain diagnostic data today is associated with sample collection, transportation and preparation. Although the tests individually can be performed in a matter of minutes, the time taken for transportation, preparation and reporting often means that results are not available for days.

Clearly, many of the tests performed within these centralised laboratories are extremely labour intensive and from start to finish have high levels of human intervention. The actual tests are usually automated and these are frequently based on optical, chemical and electrochemical methods that have been determined years (sometimes decades) ago. In the central laboratory automation invariably adds complexity resulting in expensive high maintenance equipment requiring expensive high maintenance highly skilled personnel.

There is a need for on the spot, convenient and rapid systems for clinical diagnoses. The inherent delay in existing methods frequently necessitates medical intervention prior to
definitive identification of the nature of a condition. In industrial, public health or clinical environments, such delays may have serious consequences.

Some blood sample analysis systems are described as point of care. Frequently this term is a misnomer with the analyser merely situated on the same medical complex and not actually beside the patient. These systems are often described as portable blood chemistry systems. For example a portable computer (PC) can quite easily be moved but still requires a fixed infrastructure such as table and power supply. In contrast a PDA handheld instrument can not only be easily moved it is immediately operational anywhere without modification. It does not require any infrastructure. It can effectively be used at will anywhere and anytime. There is a need for a mobile analyser system with integrated data base that can be used and accessed anywhere anytime. It will be appreciated that the most notable feature of a mobile unit is that it can, without interfering with the day to day routine of a person, be routinely carried and used at will without any form of auxiliary supporting infrastructure.

Consequently, there remains a need for truly portable, accurate, convenient analysis and diagnostic system for rapid point of care analysis.

Furthermore, sample size constrains the analysis of biological samples. Samples of tens of milliliters of blood may make little or no difference to an adult; however, it may make the world of difference to the health of an infant. Similarly when used in veterinary medicine a large biological sample may make very little difference to a large animal such as a horse but may affect the health of a smaller animal such as a rabbit. With this in mind an analysis system that requires smaller samples would be desirable.

The most frequently requested laboratory blood tests broadly fall into 2 categories, the Complete Blood Count (CBC) and the Comprehensive Metabolic Panel (CMP).

The CBC is a basic screening test which gives valuable diagnostic information about haematologic and other body systems, prognosis, response to treatment, and recovery. The CBC consists of a series of tests that determine the number, variety, percentage, concentrations and quality of blood cells (A manual of Laboratory & Diagnostic Tests,
Fischbach, 2000). Classically these consist of red blood cell count, white blood cell count (and differential), platelet count, haemoglobin concentration and haematocrit. These data can be analysed mathematically to generate the Mean Corpuscular Volume (MCV), Mean Corpuscular haemoglobin (MCH) and Mean Corpuscular concentration (MCHC). Traditionally the CBC is measured on a cytometer. Existing laboratory cytometers have a very large footprint taking up approximately 0.6m$^3$ of space. Furthermore, these instruments require skilled operators and continuous supervision. There is a further need for a miniaturized and portable cytometer system that could be used in each doctors office as a point of care instrument at home for patients with chronic disease, at all admission sites, in clinics, in underdeveloped countries, by veterinarians in the field or in places of bio-warfare agents.

The CMP is used as a broad screening tool to check for conditions such as diabetes, liver disease, and kidney disease. It is also used to monitor complications of diseases or side effects of medications used to treat diseases. The CMP is also used to monitor some known problems, such as hypertension, and drug therapies, such as cholesterol-lowering drugs (Labtestonline.org, 2001-2004 American Association for Clinical Chemistry). The CMP includes Glucose, Calcium, Albumin, Total Protein, Sodium, Potassium, Carbon Dioxide (CO$_2$), Bicarbonate, Chloride, BUN (Blood Urea Nitrogen), Creatinine, Alkaline Phosphatase (ALP), Alanine amino transferase (ALT), Aspartate amino transferase (AST) and Bilirubin. It may also include Lactate Dehydrogenase, Creatine Kinase and Gamma-Glutamyl Transferase. Various permutations and combinations of these tests are often requested, such as electrolytes [i.e. sodium, potassium, chloride and CO$_2$], U & E [urea and electrolytes], Basic metabolism panel [creatinine, glucose and BUN], Chem-7 [electrolytes and basic metabolism panel], LFT (Liver Function Tests) [ALT, ALP, AST, total protein, albumin and bilirubin]. The most frequently requested chemistry tests by general practitioners are the chem-7 [electrolytes, glucose, urea and creatinine], cholesterol or lipid panel [total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides] and thyroid function tests [T3, T4 and TSH].

There is a need for a mobile portable true point of care device with the flexibility to carry out a multitude of tests including but not limited to the (whole or part of) CMP, CBC, lipid panel and thyroid function tests. Furthermore, there is a need to have an
integrated and interactive test database whereby the physician can interpret the current test results without the need of a separate reference source. In addition to the convenience and speed that this will facilitate, there should be a marked reduction in patient and sample matching errors. If the test is carried out beside the patient and automated there will be no errors in labeling, loss of sample during transport or data entry errors.

In recent decades the art has developed a very large number of protocols, test kits, and cartridges for conducting analyses on biological samples for various diagnostic and monitoring purposes. Many devices are disclosed to carry out sample handling on the microscale. Wilding et al. (Anal. Biochem. 257: 95-100 (1998)) describe micro machined weir type filters whereby larger white cells are trapped between the weir and the covering transparent plate and only the red cells “allowed” through. A disadvantage of this system is that although it is automated to a point, it requires that the user employs an external optical device to peer into the micro machined chip to examine the trapped white blood cells. In addition to the need for human intervention, the necessary external optics makes this quite a large device.

Small devices with disposable test strips have been developed for handling biological samples and for conducting certain clinical tests. These often consist of a handheld device for measuring one parameter at a time including but not limited to glucose (US5366609) or cholesterol (US5597532). These instruments typically include an LCD display providing the user with a readout of the parameter being measured. Should the user wish to include the information within a database he/she must transcribe the readings and re enter the data on a personal computing device or network.

Other devices provide for a method to measure parameters such as blood glucose and track by means of a personal digital assistant such as a Palm. Patent application US2003176183 provides for a measurement module for glucose testing comprising:
(a) a glucose testing measurement module housing;
(b) a test strip receptacle formed in the housing;
(c) a connector portion formed in the housing and shaped to permit mechanical
removable attachment of the housing to a hand-held processing device. This device is limited by the fact that it measures one parameter at a time, for example glucose.

Patent US5968329 (Diametrics) describes a portable clinical system for providing a rapid electrochemical analysis of biological sera of interest at the point-of-care using a portable analyser unit and a multi-sensor electrochemical plug-in cartridge analyzing system. Furthermore it provides for interfacing to an external PC.

US5096669 (I-STAT Corp) describes a system comprising a disposable device and hand held reader that can perform a variety of electrochemical measurements on blood or other fluids. This device however, only carries out clinical chemistry analysis.

The concept of an integrated database within the testing device is not new. The most common methods described are systems for first collecting and storing data using an instrument on site with the patient. This stored test information can provide simplified output allowing the user to visualize trends in their condition. However, frequently the stored information requires complex algorithms or experienced diagnosis and in this instance telemetry links are described whereby information is downloaded to a central location and assessed by a clinician.

US4731726 describes a system with internal database that records a patient’s glucose readings which can then be interpreted by a clinician by means of a remote communication link. US4712562 describes a similar system that measures blood pressure.

US704366 describes a system for monitoring and reporting medical information utilizing a stand alone monitor for storing data records and transmitting the records to a remote reporting unit over a communication system.

US5724580 describes a method to formulate and manage a prognosis report at a centralized data management centre for a patient at a remote location.
Patent application US2003176183 already described incorporates a database system with which the patient can record his or her own glucose levels. These are then automatically compared to previous recordings to indicate a trend.

5 **Object of the Invention**

It is an object of the invention to provide an analytical system that can analyse microvolumes of a blood sample and produce analytical results rapidly.

10 It is another object of this invention to provide a portable analytical system that can perform clinical chemistry and haematology tests, simultaneously or separately.

It is another object of this invention to provide an analytical system that is mobile and handheld.

15 Another object is to provide easily mass produced, disposable, small cartridges/cards having miniature functional elements capable of rapid, automated analyses, in a range of applications.

20 It is a further object of the invention to provide a family of such cartridges/cards that individually can be used to implement a range of rapid tests.

It is a further object of the invention to provide a system which will not merely store results information but will compare multiple test parameters with an integrated relational database showing how the results interact with one another.

25 It is a further object of this invention to provide an interactive system, where the system suggests possible tests, performs patient trend analysis. Such a system could be used by an onsite clinician to help formulate a real-time diagnosis.

30 **Summary of the Invention**

A portable peripheral apparatus for accepting a wide array of blood analyser cartridges containing either single or multi-test panels.
According to the present invention, there is provided a portable biological fluid testing system comprising:

at least one sensor cartridge having at least one sensor,

an analyser adapted to analyse readings from said at least one sensor, said analyser comprising means for calculating cell count and means for calculating at least one analyte measurement, and

a data processor for processing said results, said data processor means comprising an interactive database.

It will be appreciated that although the analyser comprises means for calculating both cell count and at least one analyte measurement, in use it may be only necessary to calculate cell count or at least one analyte measurement. For example, in one embodiment the system may comprise one sensor cartridge comprising only one sensor adapted to take only a cell count reading.

The analyser may comprise means to connect to a pulse oximeter device.

Preferably the cartridge contains a plurality of tests to measure some predetermined construct in a fluid, such as blood.

The cartridge may contain a plurality of sensor types including Ion Selective, Amperometric, Potentiometric, Conductometric, Reflectance Spectrophotometric, Absorbance, Light Scatter, Electrophoretic, Dielectrophoretic, DC/AC Impedance and biosensors.

Preferably the cartridge comprises at least one fluid inlet port in fluid communication with said at least one sensor, and communication means for communication between said at least one sensor and said analyser.

It will be appreciated that the cartridges are capable of performing Clinical Chemistry and Haematology tests, either separately or in combination.
Preferably, the cartridge is disposable obviating the need for flushing or cleaning.

Preferably, the cartridge is a single-use, disposable cartridge. However, the cartridge may be reusable.

The cartridge may comprise a unique bar code identifier. Furthermore, the analyser may comprise means to read said unique bar code identifier.

The cartridge may further comprise means to store calibration information. The cartridge may further comprise a reservoir of calibrant in fluid communication with a bank of sensors to facilitate calibration of the system. In one embodiment, the reservoir of calibrant may be a burstable pouch. The analyser may comprise means to read information such as calibration information stored on the cartridge.

In accordance with one embodiment of cartridge, each inlet port is in fluid communication with a multiple of sensors. According to a further embodiment of cartridge, each inlet port is in fluid communication with a single sensor. In accordance with a third embodiment of cartridge, at least one inlet port is in fluid communication with a single sensor and at least one inlet port is in fluid communication with a multiple of sensors.

The cartridge may further comprise a filter such as a filter layer for filtering unwanted substances from the fluid. The filter may be located in the inlet port or may be located in a flow channel connecting the inlet port with a sensor.

The cartridge may further comprise a lysing area or layer for lysing cells to release the contents. The lysing layer may be located in the inlet port or may be located in a flow channel connecting the inlet port with a sensor.

The cartridge may further comprise a filter and lysing area for filtering unwanted substances from the fluid and lysing cells to release the contents. This area may be located in the inlet port or may be located in a flow channel connecting the inlet port with a sensor.
The cartridge may further comprise at least one flow sensor and/or at least one valve to control the flow of fluid through the cartridge.

Suitably, the cartridge further comprises an overflow reservoir for accepting excess fluid introduced into said inlet port. An outlet reservoir for storing tested fluid may also be provided.

Preferably, the cartridge further comprises driving means for driving fluid through the cartridge. The driving means may be an electric or mechanical micropump. Preferably, the analyser comprises an activating means for said micropump.

Alternatively, the driving means and actuator are both located within the analysing unit.

Alternatively, the fluid may be moved via capillary action or by means of external syringe action.

Suitably, the cartridge may contain one or more sensors designed to carry basic and comprehensive metabolic panels. These tests include but are not limited to Alanine Aminotransferase, Albumin, Alkaline Phosphatase, Aspartate Aminotransferase, Bilirubin (Total and Direct), Calcium, Carbon Dioxide (Bicarbonate), Chloride, Creatinine, Glucose, High Density Lipoprotein (HDL) Cholesterol, Low Density Lipoprotein (LDL) Cholesterol, Potassium, Protein (Total), Sodium, Total Cholesterol, Triglycerides, Urea Nitrogen (BUN), Lactate Dehydrogenase, Gamma Glutamyltransferase (GGT) and Creatine Kinase. The cartridge may also be adapted to carry out haematological tests.

The cartridge may include tests for some or all of the tests for a CBC. These include, but are not limited to red blood cell count, white blood cell count, white blood cell differential, haemoglobin concentration.

The cartridge may include tests for nutrient components such as vitamins and minerals.
The cartridge may also, but not exclusively, include tests used in veterinary medicine, for bio warfare agents, pharmaceutical testing, substance abuse, quality control, pollutant measurement, animal health, food quality such anti-biotics in agricultural products, growth enhancers in agricultural products, genetically modified foods, screening programs for neonates, children and adults, fertility testing and animal husbandry.

The cartridge may include tests for screening neonates for metabolic disorders such as PKU or heal prick test.

Preferably, the analyser is handheld.

Preferably, the analyser comprises at least one port for receiving one or more of said cartridges.

Preferably, the analyser contains a microprocessor to utilize the measured parameters to derive parameters. These derived parameters include but are not limited to LDL cholesterol and cholesterol Index, Mean Corpuscular volume (MCV), Mean Corpuscular Haemoglobin Concentration (MCHC), Mean Corpuscular Haemoglobin (MCH) and Red Cell Size Distribution Width (RDW).

Preferably, the sensor cartridge comprises at least one optical sensor and the analyser comprises an optical detection system comprising:
a light source for supplying light to said at least one optical sensor; and
an optical reader for taking a reading from said at least one optical sensor.

Preferably the analyser includes connection means and electrical circuits to perform electrical and electrochemical analysis of samples.

Where the analyser comprises an optical detection system, the cartridge’s communication means preferably comprises at least one fibre optic for communication of light between at least one optical sensor and the optical detection system in the analyser.
The communication means may further comprise electrical communication means, for communication of an electrical signal between an electrical sensor and the analyser.

In one embodiment, the analyser may further comprise a thermal stabilisation unit for stabilising the temperature of the sensors.

The analyser may be adapted to measure pulse oximetry. Preferably, the analyser comprises an attachment to measure pulse oximetry.

Preferably, the analyser device and data processor are combined so as to be a single device.

Preferably, the data processing means is a personal digital assistant (PDA). Preferably, the PDA has an interactive test database capable of providing real time diagnosis information specifically relating to the tests being carried out.

In one embodiment of the analyser, the analyser is adapted to receive said PDA. The peripheral analyser unit may include moulded flanges into which the PDA device slides.

In another embodiment the analyser may be a modified PDA with module and PDA encased within the one body.

In yet another embodiment the analyser may be so reduced in size to slot into an existing expansion slot on the PDA.

The Personal Digital Assistant (PDA) may be a Dell Axim, HP Ipaq, Palm, or a Tablet type PC such as the HP Compaq Tablet PC tc1100 or derivatives. In an alternative embodiment, the data processing means may be a phone or a watch.

The system may further comprise, as part of its construction, a bar code reader to identify a patient identification from a bar code unique to the patent for example but not limited to hospital number or social security number or equivalent.
The bar code reader may also be used to identify and verify the test cartridges.

The system may have a strap attachment or some other device such as a carrying strap, to attach the analyser to the user, thereby using the system in a hands free manner.

The system may further comprise a base station or cradle. The system may further comprise a communication point to connect it to a base station or cradle. When in communication with the cradle, batteries of the PDA and analyser can be charged. Furthermore, other computers or networks in communication with the cradle can communicate with the PDA when it is inserted. The cradle may comprise means for connection of said data processor to the Internet.

The interactive database provides for the test results to be compared to an installed test database and a possible diagnosis provided.

In using the database, a user may seek further information by clicking on a hyperlink associated with a particular term.

The database may be updated at intervals either when the analyser is in communication with the cradle or when connected to the WWW.

The data processing means may further comprise means for downloading patient record from a central medical database.

The data processing means may further comprise means for uploading patent test results to a central medical database.

The invention provides methods and devices for use in a wide range of possible tests. These may be completed rapidly, and at the conclusion of the test the cartridge can be discarded, which advantageously prevents contamination between samples, entombs potentially biologically hazardous material, and provides an inexpensive, microsample analysis.
Some of the features and benefits of devices constructed in accordance with the teachings disclosed herein are summarised below.

- The mass production of the cartridges using existing technologies allows the cartridges to be disposable and single use. This eliminates the need for flushing and washing systems further reducing the size and biohazards are reduced because of the sealed system.

- The automated nature of the device will allow for the reduction in the support infrastructure and user skill again allowing it to be used in situations previously not possible.

- Small size with no bulky instrumentation required. The smaller cartridges result in reduced shipping and storage costs. Furthermore, reduced sensor size minimises the reagent volumes, reducing reagent costs. The reduction in sensor size will also permit more sensors per unit area to be included on each cartridge allowing multiple processes to be performed simultaneously. This will not only reduce capital outlay but also will allow the device to be used where no infrastructure exists such as in developing countries or in the case of veterinary medicine beside an animal in the field. The handheld nature will allow the device to be used in many situations where minimal equipment is required such emergency rescue or the battlefield. Cost advantages will be seen not merely in monetary terms but also in the form of timely test results and the public health benefits this will facilitate.

In accordance with the preferred embodiments of the present invention, a handheld unit used in conjunction with a disposable testing cartridge may be provided for performing a variety of measurements on blood or other fluids.

The disposable cartridge may be constructed to provide a multitude of functions including cartridge sensor calibration, sample ingress, sample preparation, sample measurement and sample retention for biohazard control. In operation, the disposable cartridge may be inserted into a hand-held apparatus. Preferably, the hand held PDA controlled apparatus provides the electrical connections to the sensors, digitising of the
data and automatic control of the measurement sequence with minimal operator intervention.

According to one embodiment of the invention, the disposable device may include a casing within which are mounted a plurality of sensors and their electrical connections. The cartridge may be constructed of one or more material types such as silicon, quartz, glass, metal, plastic or polymer. It may be for example machined or injection moulded in one or more pieces. It may furthermore be constructed by the layering of laminate materials. The sensor types may include but not necessarily be limited to Ion Selective, Amperometric, Reflectance Spectrophotometric, Absorbance, Light Scatter, Electrophoretic, Dielectrophoretic, DC/AC Impedance and biosensor. The sensors generate electric signals based on the concentration of specific substances in the fluid sample tested. Preferably, the hand-held reader includes an opening in which the disposable device is received so that electrical, optical or mechanical contacts on the cartridge become in communication with corresponding contacts within the opening of the hand held reader device. The PDA controlled apparatus may automatically processes the tests in a predetermined sequence. Preferably, the hand held PDA controlled reader records the electric potentials produced by the sensors. These electrical potentials may be digitised by the handheld apparatus and processed by the handheld computer device. This information in conjunction with the interactive database may be immediately available for use in medical evaluation and diagnosis.

While use of the invention is particularly advantageous in the medical environment and will be described in that context, it will be appreciated that the invention may be practiced in any situation where it is desired to perform chemical analyses of fluid samples at speeds which approach real-time.

**Brief Description of the Drawings**

These and other features of the present invention will better understood with reference to the following drawings wherein:

Figure 1 is a flow chart representing a system according to the present invention.
Figure 2 is a perspective view of a first embodiment of cartridge, analyzer and data processor of the system of Figure 1.

Figure 3 is a perspective view of a second embodiment of cartridge, analyzer and data processor of the system of Figure 1.

Figure 4 shows a plan, side and perspective view of the assembled cartridge, analyzer and data processor of Figure 3.

Figure 5 is a perspective view of a third embodiment of cartridge, analyzer and data processor of the system of Figure 1.

Figure 6 is a perspective view of an embodiment of the system of Figure 1.

Figure 7a is a detailed view of the analyzer of Figure 3.

Figure 7b is a detailed view of the analyzer of Figure 2.

Figure 7c is a detailed view of the analyzer of Figure 5.

Figure 8 is a perspective view of the assembled analyser and cartridge of Figure 2.

Figure 9a is a perspective view of the assembled analyser and cartridge from Figure 3.

Figure 9b is a perspective view of the analyser from Figure 3 with 2 cartridges inserted.

Figure 10 is a perspective view of the assembled analyser and cartridge from Figure 5.

Figure 11a is a perspective view of the assembled cartridge, analyzer and data processor of Figure 3.

Figure 11b is a perspective view of the assembled cartridge, analyzer and data processor of Figure 5.

Figure 11c is a perspective view of the assembled cartridge, analyzer and data processor of Figure 2.

Figure 12 shows one embodiment of cartridge of the system of Figure 1.

Figure 13 shows a second embodiment of cartridge of the system of Figure 1.

Figure 14 shows a third embodiment of cartridge of the system of Figure 1.

Figure 15 shows a fourth embodiment of the cartridge of the system of Figure 1.

Figure 16 is a screenshot from the data processor of Figure 1 following tests.

**Detailed Description of the Drawings**

Figure 1 illustrates the general concepts of the system in accordance with one embodiment of the invention. Three hardware elements comprise the basic analyser; cartridge, analyser and data processor. The analyser and data processor may be
incorporated into the one body. The analyser houses the electronics and optics (or whatever system is being used) necessary to read the tests performed. The analyser itself provides the port of entry for one or more cartridges. These cartridges contain the sensors, chemistries and other necessities to analyse the analyte inserted into the cartridge. The analyser is linked to a handheld computer device. The basic system can work alone, with just these three parts and the associated software, or the data processor can be connected to an auxiliary system such as a PC, computer network or any other system. The use of the World Wide Web or other up to date sources of information will allow for regular updates and for further information searches if required.

Figure 2 shows a first embodiment of the analyser, data processor and cartridge of the system of Figure 1. The system consists of an analyser 1, data processor 2 and cartridge 3. In this embodiment the data processor is a PDA. The analyser 1 houses a mechanism to link to the data processor, which in this embodiment is via the compact flash slot. This may be through any means of communication including but not exclusively to special adapters, USB, Firewire, and wireless communication such as but not exclusively Bluetooth or infra red. The analyser also has one or more slots to accept cartridges. The cartridge 3 houses one or more sensors capable of testing for one or more analyte. The cartridge contains an inlet port, to enable the insertion of analyte into the system. The cartridge is enclosed. The data from the sensors in the cartridge are output to the analyser and data processor while the analyte is entombed within the cartridge. No part of the analyte comes in contact with any external part of the analyser. In this embodiment the data processor 2 is a Pocket PC. The data processor contains a software data bank to facilitate in data analysis of the analyte being tested. The data processor also houses the necessary software and hardware to communicate with the auxiliary interface.

Figure 3 shows a second embodiment of the analyser 5, data processor 2 and cartridge 3. The analyser 5 houses a mechanism to link to the data processor. The cartridge 3 houses one or more sensors capable of testing for one or more analyte. In this embodiment the data processor 2 is a Pocket PC. The data processor contains a software data bank to facilitate data analysis of the analyte being tested.
Figure 4 is three different angles of the embodiment of the basic system described in figure 3. Figure 4a illustrates the top end of the system with data processor 2, analyser 5 and two cartridges 3. Figure 4b again depicts the second embodiment of the system from the side angle, with analyser 5, data processor 2 and again two cartridges 3. Figure 4c depicts the second embodiment of the system from the front, with data processor 2, cartridge 3 and analyser 5.

Figure 5 demonstrates a third embodiment of the basic system. The cartridge 3 slots into the analyser 6 which attaches to the data processor via the compact flash slot. As for the previous embodiments communication between the data processor and analyser can occur through a variety of standard or specialised communication ports and or can be via wireless communication.

Figure 6 shows a fourth embodiment of the system of Figure 1. In this embodiment the computer and the analyser are housed as one unit 7. The cartridge 3 slots into an opening in the outer casing. The electronics, optics, mechanics etc. necessary to read and analyse the cartridge are housed within the outer casing of the single unit. The handheld all in one instrument may be accessed via a touch screen 8 or touch keys 9. The reverse of the instrument contains an attachment device or strap 9, by which the analyser can be attached to the person. Embodiments one, two, and three may also contain an attachment device.

Figure 7a illustrates the analyser 5 from figure 3. Figure 7b illustrates the analyser 1 as shown in figure 2 and figure 7c illustrates the analyser 6. In these embodiments the analysers all attach to the data processor device via standard serial or expansion communication ports 11 and compact flash slot 12. In another embodiment the analyser may communicate via wireless communication or via another standard or specially designed communication port or device.

Figure 8 illustrates the analyser 1 from figure 2 with a cartridge 3 inserted into it.

Figure 9a illustrates the analyser 5 from figure 3 with a cartridge 3 inserted into it while figure 9b illustrates the analyser 5 with 2 cartridges inserted into it.
Figure 10 illustrates the analyser 6 from figure 5 with a cartridge 3 inserted into it.

Figure 11 illustrates three embodiments of the system with all parts of the basic analyser system attached, data processor, analyser and cartridge.

The cartridge may consist of almost any configuration of sensors. The cartridge may contain more than one type of sensor. In the embodiment of Figure 12a, the cartridge houses 8 sensors. The cartridge may contain more or less than this number of sensors. In figure 12b the sensors are all electrochemical. In figure 12c the sensors are all optical. In figure 12a there is a mixture of electrochemical and optical sensors. The electrochemical sensors 13 contain two electrodes, they may alternatively contain more or less than this number. The cartridge may also contain a reference and or a counter electrode, not illustrated in these embodiments. The cartridge may consist of a shape consistent with a credit card. One end of the outer casing of the cartridge is molded for easy handling, which in this embodiment is a thumb handling mould 15. The micro flow channels 16 within the cartridge may, where necessary, be designed so as to control the passage of test fluid through the system. This affords the sequential addition of reagents in a controlled fashion. The pattern of micro channels in this embodiment is radial, from a central pore 4. Analyte is inserted into the cartridge through the central pore. This may also house filters or filter layers to remove unwanted particles or chemicals. Alternatively this layer can be used to modify the sample to be tested so that it can be accurately or more efficiently analysed by the sensors within the cartridge.

The cartridge may contain conductive materials, either in individual areas or in totality, to facilitate the conduction of heat/cold when an analyte is to be analysed at a required temperature.

Analytical devices having micro flow channels can be manufactured from a solid silicon or quartz substrate using existing semiconductor manufacturing processes. These processes include photolithography, etching, diffusion, on implantation and film deposition (see May and Sze, Fundamentals of Semiconductor Manufacturing, 2004). Other materials such as polymers may be used. Polymer cartridges can be machined or
embossed from a solid substrate or injection molded. Alternatively, they can be constructed by layering of multiple laminates.

Flow channels of various widths and depths can be fabricated with micro scale dimensions to handle fluid samples. The capacity of the devices is very small and therefore this reduces the sample size required and the quantity of reagents used.

The sample may be injected into the device, be pumped using micropump or move by means of capillary action.

To enable the cartridge to be disposable certain components of the system will have to remain off cartridge. For example for the optical detection system it will be necessary to keep the light source within the reader unit and channel it into the disposable cards by means of fibre optics or other means known in the art. With regard to the micropump it may also be necessary to keep certain components off the cartridge to reduce size and cost. For example if a mechanical pump is inserted into the cartridge that relies on the depression of a diaphragm or the like, it may be advantageous to locate the actuator in the reader device. This will then come into contact with the diaphragm when the cartridge is inserted. The cartridge will also have the facility for thermal stabilisation where specific tests require.

In the embodiment of Figure 13a, the cartridge houses 8 sensors, in figure 13b these are all electrochemical, figure 13c the sensors are all optical, figure 13a there is a mixture of electrochemical and optical sensors. The cartridge consists of a shape consistent with a credit card. One end of the outer casing of the cartridge is molded for easy handling, which in this embodiment is a thumb handling mould. The micro flow channels within the cartridge 16 may, where necessary, be designed so as to control the passage of test fluid through the system. In this embodiment the distance from the central pore to the sensor is equal for all sensors. This affords the sequential addition of reagents in a controlled fashion.

In this embodiments of Figure 14, the cartridge houses 8 sensors. In figure 14a these are all electrochemical, figure 14b the sensors are all optical. It is envisaged that a cartridge
will contain some electrochemical and some optical sensors. Figure 14c illustrates the reverse of the cartridge. Here there is a bar code 17, which in this embodiment is a 2D barcode. Ideally the cartridge incorporates a bar code 17 or some other information containing feature such as a microchip, containing relevant information which may include but is not exclusive to test identity, test profile, best before date. This area may also store data relating to standard curves for specific batches of sensors. A bar code or a data storage device could be added to any embodiment of cartridge. The micro flow channels within the cartridge 4 may, where necessary, be designed so as to control the passage of test fluid through the system. This affords the sequential addition of reagents in a controlled fashion. In this embodiment the pattern of flow is through one sensor to the next.

In any embodiment the inlet port/port’s may include a septum which may be pierced with syringe needle or syringe nozzle. The sample may be propelled through the channels by means of capillary action or pumped via micro pumps, or by means of external syringe action.

In any embodiment the device includes a solid substrate fabricated with inlet ports, sample channels and sensor devices and communication means. The cartridge may also contain a variety of atmospheric sensors and or regulators such as temperature, moisture, light, oxygen etc.

Figure 15a shows a fourth embodiment of cartridge with twenty-five inlet ports 101-125, micro channels to sensors a-x, micro pump A1, flow control sensor and valves A2, lysing chamber A3 and optical sensors A4. Electrical contacts are shown at A6 and the proposed connection between the pump actuator (located in the reader device) and the micro pump will be in close proximity to A1. Furthermore the proposed optical interface (linking light source and cartridge) will be located in close proximity to A4.

Figure 15b shows a fifth embodiment of cartridge with two inlet ports 201-202, micro channels to sensors A-AE, micro pump A1, flow control sensor and valves A2, lysing Chamber A3 and optical sensors A4.
Figure 15c shows a sixth embodiment of cartridge composed of a combination of multiple inlet ports-multiple sensors and single inlet port-multiple sensors 301-316, micro channels to sensors A-Z, micro pump A1, flow control sensor and valves A2, lysing chamber A3 and optical sensors A4.

Figure 15d shows seventh embodiment of cartridge composed of a combination of single inlet port-multiple sensors 401-402, micro channels to sensors A-Z, micro pump A1, flow control sensor and valves A2, lysing chamber A3 and optical sensors A4.

Figure 16 shows one possible screenshot presented to user following tests. The analyte measured is on the left. A simple indication of whether this is normal or not (Y) or (N) respectively, is given and the normative range is presented. The analytes on the left are shown as hyperlinks. By selecting a link the user will be presented with Critical Values, Test Explanations, Interfering Factors etcetera. By clicking on the hyperlink “Interaction of Results” the user will be presented with a possible diagnosis or suggestions for further patient testing.

Example of use

For example to carry out an electrolyte panel on a subject’s blood the medic first scans the patient’s wristband with the bar code reader mounted at the front of the device. This automatically brings up the patient name and id. This is verified by the medic by confirming the on screen name with the patient (if the patient is capable) or by other means. The medic then withdraws a blood sample from the subject. This is then injected into the inlet port of the cartridge. Microfluidic channels guide the sample to the sensors. The sensors detect the level of ions for example in the blood. The analogue electrical signals from the sensors are digitised by the electronics within the analyser and data processor apparatus. This then produces a signal that the data processor can read and display the result on the screen. The operator can select further information by means of links or drop down menus on the data processor screen that can help interpret the results or indeed suggest a diagnosis. The results can then be added by paper or electronic means to the patient record if desired.

Upon completion of the process, the medic removes the cartridge from the reader and
simply disposes of it in an appropriate way. An advantage of this is that the biohazard material is entombed within the cartridge. The reader is then ready to perform another measurement which is initiated by the insertion of another disposable device.

In addition to the test management control software, the system comprises an integrated test reference database. This software is not simply installed on the same device to act in a passive fashion but to interact with the test results should the physician require it.

The screen also has drop down menus or hotlinks for further information. For example, if the cartridge was configured to test Sodium, Potassium and Calcium the user could access further information such as Critical Values, Test Explanations, Interfering Factors etcetera by touching the associated hyperlinks which would be activated by touching the words, Sodium, Potassium and Calcium. It is also envisaged that certain terms can have an associated hyperlink to provide more information. For example, consider the suggested diagnosis Hyperaldsteronism, then clicking on the term would provide further information. Furthermore, it is envisaged that should it be required the option will be there to seek further information on the World Wide Web. A facility to upload most recent updates of test references will be provided that can be installed on the mobile device while resting on the cradle or when connected to the web. The database will be customised for each country served in terms of relevance and language.

For example should the Interaction of Results hyperlink be pressed, the following may appear on the screen:

Increased Levels of Potassium + Increased levels of Sodium. This may suggest

- Excessive dietary intake of the two ions or
- IV administered provided too much of each of the two ions.

Or if there were:
Decreased Levels of Potassium + Increased Levels of Sodium. This might suggest

- Hyperaldsteronism or
- Cushings Syndrome

Or if there were:
Decreased Levels of Potassium + Decreased Levels of Sodium. This might suggest
  • Diuretic use or
  • Gastrointestinal problems such as diarrhoea

The words “comprises/comprising” and the words “having/including” when used herein
with reference to the present invention are used to specify the presence of stated
features, integers, steps or components but does not preclude the presence or addition of
one or more other features, integers, steps, components or groups thereof.

It is appreciated that certain features of the invention, which are, for clarity, described in
the context of separate embodiments, may also be provided in combination in a single
embodiment. Conversely, various features of the invention which are, for brevity,
described in the context of a single embodiment, may also be provided separately or in
any suitable sub-combination.
Claims

1. A portable biological fluid testing system comprising:
   at least one sensor cartridge having at least one sensor,
   an analyser adapted to analyse readings from said at least one sensor,
   said analyser comprising means for calculating cell count and means for
   calculating at least one analyte measurement, and
   a data processor for processing said results, said data processor means
   comprising an interactive database.

2. The system of claim 1 wherein said at least one sensor is selected from the types
   including Ion Selective, Amperometric, Conductometric, Potentiometric,
   Reflectance Spectrophotometric, Absorbance, Light Scatter, Electrophoretic,
   Dielectrophoretic, DC/AC Impedance and biosensors.

3. The system of any preceding claim wherein said at least one sensor cartridge is
   disposable.

4. The system of any preceding claim wherein said at least one sensor cartridge is a
   single-use, disposable cartridge.

5. The system of any preceding claim wherein said at least one sensor cartridge is
   reusable.

6. The system of any preceding claim wherein said at least one sensor cartridge
   comprises a unique bar code identifier.

7. The system of claim 7 wherein said analyser comprises means to read said
   unique bar code identifier.

8. The system of any preceding claim wherein said at least one sensor cartridge
   further comprises means to store calibration information.
9. The system of claim 8 wherein said analyser further comprises means to read calibration information stored on said at least one sensor cartridge.

10. The system of any preceding claim wherein said at least one sensor cartridge further comprises:

at least one fluid inlet port in fluid communication with said at least one sensor, and

communication means for communication between said at least one sensor and said analyser.

11. The system of claim 10 wherein each inlet port of said at least one sensor cartridge is in fluid communication with at least one sensor.

12. The system of claim 10 wherein at least one inlet port is in fluid communication with a single sensor and at least one inlet port is in fluid communication with a multiple of sensors.

13. The system of any preceding claim wherein said at least one sensor cartridge further comprises a filter for filtering unwanted substances from a fluid.

14. The system of claim 13 wherein said filter is located in a fluid inlet port.

15. The system of claim 13 wherein said filter is located between a fluid inlet port and a sensor.

16. The system of any preceding claim wherein said at least one sensor cartridge further comprises a lysing area for lysing cells to release their contents.

17. The system of claim 16 wherein said lysing area is located in a fluid inlet port.

18. The system of claim 16 wherein said lysing area is located between a fluid inlet port and a sensor.
19. The system of any preceding claim wherein said at least one sensor cartridge further comprises at least one flow sensor to sense the flow of fluid through said at least one sensor cartridge.

20. The system of any preceding claim wherein said at least one sensor cartridge further comprises at least one valve flow to control the flow of fluid through said at least one sensor cartridge.

21. The system of any preceding claim wherein said at least one sensor cartridge further comprises a reservoir of calibrant in fluid communication with a bank of sensors to facilitate calibration of said system.

22. The system of claim 21 wherein said reservoir of calibrant is a burstable pouch.

23. The system of any preceding claim wherein said at least one sensor cartridge further comprises an overflow reservoir for accepting excess fluid introduced into a fluid inlet port.

24. The system of any preceding claim wherein said at least one sensor cartridge further comprises an outlet reservoir for storing tested fluid.

25. The system of any preceding claim wherein said at least one sensor is adapted to carry out basic and comprehensive metabolic test panels.

26. The systems of any preceding claim wherein said at least one sensor cartridge is adapted to carry out haematological tests.

27. The system of any preceding claim further comprising driving means for driving fluid through said at least one sensor cartridge.

28. The system of claim 27 wherein said driving means is an electric or mechanical micropump.
29. The system of claim 27 or claim 28 further comprising an actuator for activating said driving means.

30. The system of claim 29 wherein said driving means and said actuator are both located within said analyser.

31. The system of any of claims 1 to 26 wherein fluid is moved through said at least one sensor cartridge via capillary action.

32. The system of any preceding claim wherein said system is handheld.

33. The system of any preceding claim wherein said analyser comprises at least one port for receiving said at least one sensor cartridge.

34. The system of any preceding claim wherein said analyser further comprises a microprocessor to utilise measured parameters to derive parameters.

35. The system any preceding claim wherein said analyser further comprises electrodes and electrical circuits to perform electrical and electrochemical analysis of samples.

36. The system of any preceding claim wherein said at least one sensor cartridge comprises at least one optical sensor and said analyser comprises an optical detection system comprising:

a light source for supplying light to said at least one optical sensor; and

an optical reader for taking a reading from said at least one optical sensor.

37. The system of any preceding claim wherein said analyser further comprises a thermal stabilisation unit for stabilising the temperature of said at least one sensor.
38. The system of claim 36 or claim 37 wherein communication means in said cartridge comprises at least one fibre optic for communication of light between said at least one optical sensor and said optical detection system.

39. The system of any of claims 3 to 35 wherein said communication means further comprises electrical communication means for communication of an electrical signal between said at least one sensor and said analyser.

40. The system of any preceding claim wherein said analyser is adapted to measure pulse oximetry.

41. The system of any preceding claim wherein said analyser and said data processor are combined so as to be a single device.

42. The system of any preceding claim wherein said data processor is an independent unit.

43. The system of claim 42 wherein said analyser is adapted to receive said data processor.

44. The system of claim 43 wherein said analyser unit comprises moulded flanges into which said data processor slides.

45. The system of any preceding claim wherein said data processor is a personal digital assistant (PDA).

46. The system of claim 45 wherein said analyser is adapted to be insertable into an existing port of said PDA.

47. The system of any of claims 1 to 44 wherein, said data processor is a personal computer (PC).

48. The system of any of claims 1 to 44 wherein, said data processor is a telephone.
49. The system of any of claims 1 to 44 wherein, said data processor is a watch.

50. The system of any of claims 1 to 44 wherein said analyser is a modified PDA comprising said data processor.

51. The system of any preceding claim wherein said interactive database is capable of providing real time diagnosis information specifically relating to the tests being carried out.

52. The system of any preceding claim wherein said interactive database comprises means for comparing test results with an installed test database to provide a possible diagnosis.

53. The system of any preceding claim wherein said data processor comprises means for updating said interactive database at intervals.

54. The system of any preceding claim wherein said data processor further comprises means for downloading a patient record from a remote central medical database.

55. The system of any preceding claim wherein said data processing means further comprises means for uploading test results to a central medical database.

56. The system of any preceding claim further comprising a bar code reader.

57. The system of any preceding claim further comprising a carrying strap.

58. The system of any preceding claim further comprising a base station or cradle.

59. The system of claim 58 wherein said cradle comprises means for connection of said data processor to the Internet.
60. A system substantially as described herein with reference to and as shown in any one or more of the accompanying drawings.
Figure 1

Basic System

- Analyser
- Cartridge

PDA
Standalone
Or connect via wireless
or hot-sync to

Software
- Test menu
- Results analysis
- Profile and trend analysis
- Suggested
diagnosis/treatment/lifestyle
alterations
- Securely send data where required

Auxiliary Interface

- Desktop PC
- Networks
- Printers,

Lab information systems,
- Patient data bases
- www for online updates
10/13

Insert into analyser

Figure 12

Figure 13
Figure 14
### Settings

**Patient name:** John Smith  
**Patient ID:** 990099990  
**Sex:** Male  
**Age:** 55

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<th>TEST</th>
<th>RESULT</th>
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<td>Potassium</td>
<td>5.5</td>
<td>Y</td>
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<td>Sodium</td>
<td>138</td>
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<td>(136 - 145 mmol/L)</td>
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<td>BUN</td>
<td>5</td>
<td>Y</td>
<td>(3.6 - 7.1 mmol/L)</td>
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<td>Calcium</td>
<td>2.5</td>
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<td>(2.35-2.75 mmol/L)</td>
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<td>Calcium</td>
<td>1.25</td>
<td>Y</td>
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<td>Chloride</td>
<td>103</td>
<td>Y</td>
<td>(98-106 mmol/L)</td>
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<td>Bilirubin total</td>
<td>12.1</td>
<td>Y</td>
<td>(5.1 - 17 µmol/L)</td>
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<td>Bilirubin indirect</td>
<td>7.6</td>
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<td>Glucose</td>
<td>416</td>
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<td>Creatinine</td>
<td>85</td>
<td>Y</td>
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<td>Total cholesterol</td>
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<td>Y</td>
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<td>HDL</td>
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<td>AST</td>
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<td>Y</td>
<td>(0 - 0.58 µg/kL)</td>
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<td>Y</td>
<td>(4.7 - 6.1 x 10^12/L)</td>
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<td>MCV</td>
<td>85</td>
<td>Y</td>
<td>(80 - 90 µm^3)</td>
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<td>MCH</td>
<td>28.2</td>
<td>Y</td>
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<td>MCHC</td>
<td>43%</td>
<td>Y</td>
<td>(32% -36%)</td>
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<td>WBC</td>
<td>7</td>
<td>Y</td>
<td>(5 - 10 x 10^3/L)</td>
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<td>Neutrophils</td>
<td>63</td>
<td>Y</td>
<td>(55 - 70%)</td>
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<tr>
<td>Lymphocytes</td>
<td>35</td>
<td>Y</td>
<td>(20 - 40%)</td>
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<tr>
<td>Monocytes</td>
<td>3</td>
<td>Y</td>
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<tr>
<td>Eosinophils</td>
<td>3</td>
<td>Y</td>
<td>(1 - 4%)</td>
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<td>Basophils</td>
<td>75</td>
<td>Y</td>
<td>(0.5 - 1%)</td>
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<td>Hemoglobin</td>
<td>10.1</td>
<td>Y</td>
<td>(8.7 - 11.2 mmol/L)</td>
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<td>Hematocrit</td>
<td>42</td>
<td>Y</td>
<td>(0.42 - 0.52 volume fraction)</td>
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<tr>
<td>Thrombocytopenia</td>
<td>145</td>
<td>Y</td>
<td>(51-154 mmol/L)</td>
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<tr>
<td>TSH</td>
<td>7</td>
<td>Y</td>
<td>(2 - 10 mU/L)</td>
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<tr>
<td>SpO2</td>
<td>98</td>
<td>Y</td>
<td>(60-100bpm)</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>78</td>
<td>Y</td>
<td>(60-100bpm)</td>
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**Figure 16**
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. G01N15/14

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 A61B

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**

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<td>A</td>
<td>US 5 980 830 A (SAVAGE ET AL) 9 November 1999 (1999-11-09) column 3, line 9 - column 5, line 10; figures 1-5</td>
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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
- P*: 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
- A*: document member of the same patent family

**Date of the actual completion of the international search**

25 July 2006

**Date of mailing of the international search report**

01/08/2006

**Name and mailing address of the ISA**

European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk
Tel: (31-70) 340-2040, Tx: 31 651 epo nl, Fax: (31-70) 340-3076

**Authorized officer**

Wilhelm, J
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