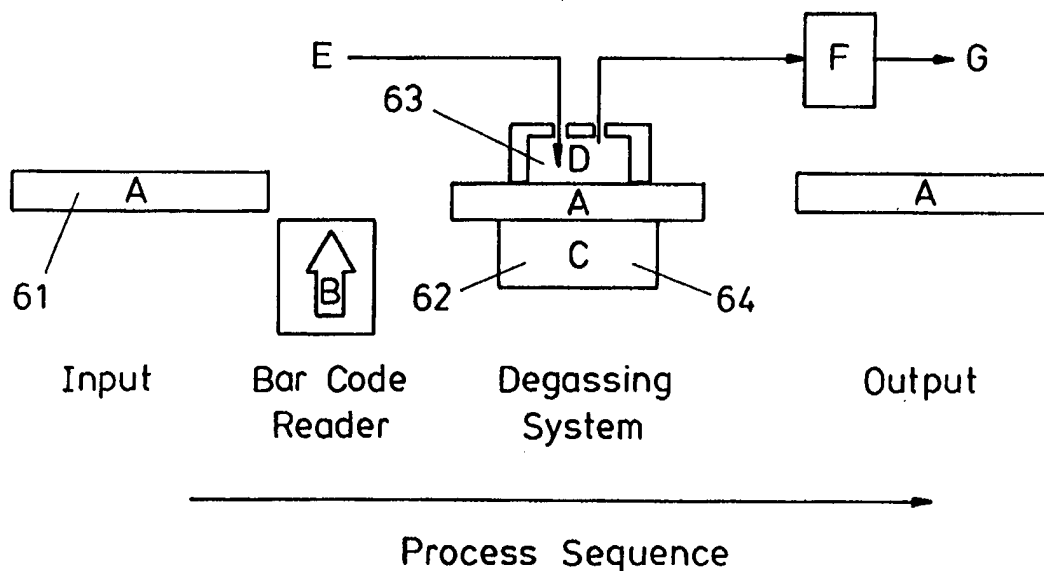




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(54) Title: A CHEMICAL SENSING SYSTEM**(57) Abstract**

A system for sensing chemicals comprises a sensor collecting means for collecting chemical species, removal means for removing the species and presenting them to the sensor, and interpretation means to interpret information obtained. The system advantageously comprises a gas permeable membrane situated in the wall of a vessel having an appropriate pore size relating to the species to be sensed.

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A CHEMICAL SENSING SYSTEM

This invention relates to a system for measuring chemicals in a test material and particularly relates to a system for measuring chemicals through use of array based chemical sensors.

It is known that measuring chemical species in operational situations presents a problem of dealing with unknown interferants which may be present in the environment. The result of such unknown interferants is, with many known systems undefined. This renders such systems unsuitable for process critical applications.

The measurement of chemical species often presents problems when the analytes which are of interest in diagnostic situations are present in relatively low concentrations when compared to ambient background materials.

In gas sensing situations, the excessive background material is usually water vapour. This often leads to impaired analytical results and can prevent any useful information from being obtained.

This is a particular problem when dealing with biological systems such as breath testing and microbial identification where the gases tend not only to be saturated with water vapour but tend to be at temperatures above ambient. This leads to the secondary problem of condensation which can further jeopardise the analytical outcome.

According to the present invention there is provided a system for sensing chemicals, the system comprising:

- a sensor;
- collecting means for collecting chemical species;
- removal means for removing the species and presenting them to the sensor; and
- interpretation means to interpret the information obtained.

According to a second aspect of the present invention there is provided a method for chemical sensing using a system

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according to the first aspect of the present invention.

According to a third aspect of the present invention there is provided a system for obtaining chemicals from gaseous liquid or solid samples, the system comprising:

- a gas permeable means;
- a chemically absorbent material;
- sealing means for sealing the absorbent.

Preferably, the system further comprises means for identifying the sample.

Conveniently the means for identifying the sample comprises a bar code.

Advantageously the system further comprises means for presenting a sample to analytical means for subsequent analysis.

Preferably, the collecting means comprises means for entrapping a chemical species.

Conveniently the interpretation means comprises a pattern recognition algorithm.

By means of the present invention, test chemicals are presented to the entrapment means which means is capable of absorbing the materials of interest, enabling preconcentration of the species if required, and retaining the material for subsequent analysis.

The system further comprises means for progressively removing either serially or in parallel the entrapped materials. The information obtained is logged, together with the response of the adjacent chemical sensing system for subsequent analysis.

The response of the chemical sensing system is a function of the removal procedure described hereinabove is analysed and information obtained on the test chemicals.

Advantageously the system according to the present invention comprises a gas permeable membrane situated in a wall of a vessel, container or conduit. The membrane is thus situated in the wall of a conveniently mechanically rigid structure within which the material to be analysed is restrained.

Advantageously the gas permeable membrane has a pore size sufficiently small to retain bacteria in the case of materials which are suspect to microbial degradation.

The membrane further comprises a detector strip comprising a chemically absorbent material deposited on a gas impermeable backing matrix. Further, the membrane comprises a means to provide a gas tight seal to the gas permeable membrane of a sample restrainer and means to provide adhesion to the sample restrainer.

The system further comprises means to remove species in the absorbent material for subsequent presentation to analytical means.

In a particular embodiment of the invention a detector strip is adhered to a suitable point in a sample handling system such as the lid of a petri dish or sample vial or a conduit or mouthpiece for a breath sample. A detector strip is positioned over a permeable membrane window.

After appropriate exposure time the detector strip is removed and placed in a strip developer which removes the materials absorbed on the detector strip. This may be achieved by heating the strip and passing a suitable carrier gas over the strip to sweep the materials off.

Conveniently, the system further comprises preconcentration means to concentrate the removed materials before presenting them to the appropriate analytical instrumentation.

Embodiments of the invention will now be further described by way of example only with reference to the accompanying drawings in which:

Figure 1 is a schematic representation of a serial instrument suitable for forming part of a system according to the present invention;

Figure 2 is a semi-parallel instrument suitable for forming part of a system according to the present invention;

Figure 3 is a parallel instrument;

Figure 4 is a detailed example of use of the system according to the present invention;

Figure 5 is a schematic representation of a detector strip forming part of a device according to the present invention; and

Figure 6 is a schematic representation of a method according to the present invention.

Referring to Figure 1, a system according to the present invention designated generally by the reference numeral 1. The system comprises an entrapment means 2 used to capture materials in the test material. In the case of liquid and solid samples the entrapment system could be replaced by a temperature ramp. This would have the effect of modulating the gas phase concentration of chemical species.

The entrapment means 2 may comprise a custom made absorbent material or a commercially available solid phase extraction material or a standard trap material packed into a column or applied as a thick layer to a flat plate or adhered to any other suitable support. The absorbent material is held at a constant temperature and the test material is passed over or through the absorbent material for a fixed period of time.

Once the entrapment has been effected, the absorbed material is desorbed by desorption means 3 before being swept onto a chemical sensor 4. A chemical sensor comprises an array of gas sensors. The desorption is effected in stages, the flow rate sweeping the entrapment device being held constant. It is important to ensure that the concentration of the desorbed materials is modified by this procedure and that the conditions of the desorption process are retained for subsequent processing.

The desorption process does not rely on a chromatographic effect as in gas chromatography for example, but simply the modification of the concentration of the analytes as a function of their absorption onto the trap. In other words it is not necessary to separate out the individual components of the test material completely.

This process may take the form of stepping up the temperature of the entrapment device in stages as shown in Figure 1, or may be through use of a continuous temperature

ramp (not shown).

The response of the chemical sensor 4 is monitored as a function of the desorption procedure. The two data sets relating to the desorption process and the response of the chemical sensor are passed to an information processing engine 5.

The data processing engine 5 employs statistical techniques such as rank annihilation factor analysis and trilinear decomposition (RAFA, GRAM and TLD) in order to obtain information from the combination of data from the desorption process and the chemical sensor. This enables analysis of the analytical data from the chemical sensor even in the presence of unknown chemical species (interference) and thus overcomes a serious problem with chemical sensors in applications where unknown materials may be encountered.

Referring to Figure 2, a semi-parallel device according to the present invention is designated generally by the reference numeral 2.

In the device 20, rather than having a single entrapment/absorption device as shown in Figure 1, there is a plurality of entrapment devices 22 and absorption devices 24 which are set to different conditions. The entrapment systems may be held at constant conditions or simultaneously desorbed and gated with a single sensor unit 22. This enables the measurements to be made more rapidly. A processing engine 26 analyses the two sets of data from devices 22, 24.

Referring to Figure 3 a fully parallel device is designated generally by the reference numeral 30. Here, not only are there a number of entrapment devices 31 and desorption devices 32 but there are also a number of chemical sensors 33. The entrapment devices may be held at constant conditions or simultaneously desorbed, for example if there are less chemical sensing units than entrapment devices then again the outputs will need to be gated with the common sensing units. This enables measurements to be made still more rapidly.

The entrapment system 32 may be used in conditions where direct measurement may be difficult, in particular whilst

making biological measurements where condensates or diffusion characteristics may make direct measurements difficult to make. For example, a sample of a patient's breath or a biological culture may be made using an entrapment device (a chemical photograph) which may be protected by a gas permeable membrane, the gases being absorbed into the material and presented for subsequent analysis.

Referring to Figure 5, a detector strip system suitable for use in such a membrane system is shown and designated generally by the reference numeral 50. The gas permeable membrane 51 is an integral part of a retainer wall enclosure which allows materials from the internal environment 52 to pass through. This may be constructed using for example 100 μm thick membrane, although any material capable of permitting gases to pass through whilst retaining the required mechanical properties may be employed. This may be heated either directly or indirectly to prevent unwanted condensation (normally in cases where the materials under test are above ambient temperatures). These test materials permeate through the membrane and are absorbed into the entrapment system. The entrapment system may comprise for example a thick tenax which is a standard chemical absorbent which may be printed onto the backing material 55. The entrapment system 53 is supported by the backing material 55 which offers a suitable mechanical support and is resistant to gaseous diffusion (preventing the entrapment system from drawing materials through the backing materials). The backing material may be a metallised material or metal foil although any material providing an appropriate barrier to gas transport whilst offering the desired mechanical properties may be employed. The material is sealed by means of seal 54 to the body of the retainer 56. The seal is preferably capable of violation without comprising the integrity of the retainer and is resistant to gaseous diffusion.

The entrapment system is sealed to the gas permeable membrane providing a gas-tight seal and in the preferred embodiment can be broken by pulling the detector strip away from the restrainer body without violating the integrity of the

membrane itself.

The seal 54 comprises an adhesive which is compatible with the backing material, the restrainer and the membrane such that the backing material is held in place and capable of removal when desired. Chemical materials within the restrainer are exchanged across the membrane into the entrapment system without violating the integrity of the contents of the restrainer.

Temperature and the time of exposure will determine the degree of exchange.

The device further comprises an identifier in the form of a bar code on the reverse side of the detector strip.

Referring to Figure 6 the method of analysis is schematically demonstrated. A detector strip 61 is removed from the restrainer 56. It is usually removed by being torn off in the fashion of a medical sticking plaster without violating the membrane or contents.

A bar code on the reverse side of the strip may be read before further processing. The detector strip 55 is then degassed by thermal means using for example thermal desorption forming part of a degassing system 62 which raised the temperature of the entrapment system resulting in the desorption of all absorbed species.

The system comprises a hood 63 which moves down impressing upon the top surface of the detector strip forming a seal and impinging it upon the base plate 64. The back side of the strip is then heated by the base plate 64 to remove the absorbed materials.

The released materials are swept from the hood using an appropriate carrier gas. This is effected by heating the mechanical parts of the system to reduce absorption to internal surfaces. The surfaces are preconcentrated using ciro-focusing.

The resultant material is then presented to appropriate analytical instrumentation. This takes the form of a gas chromatograph/mass spectrometer instrument for example. The detector strip is then output from the system.

The system may be adjusted to suit any particular analytical problem. This may be achieved by varying the temperature during the heating process using temperature wrapping techniques for example which may enable the disposal of certain proportions of the degassed materials.

Referring to Figure 4 a detailed description of a gas sensing system according to the present invention is described. The following steps are carried out:

1. A test gas is drawn through a glass sorption tube 40 which is approximately 5 mm in diameter and 50 mm long which is packed with activated charcoal which serves as an absorbent material.

The flow rate of the test gas is approximately 200 sccm and the duration of the procedure is approximately 15 minutes. The temperature of the sorption tube is approximately 20°C. The flow rate, duration and temperature are controlled during the procedure. This phase constitutes the preconcentration stage in which the test gas is trapped on the sorbent material.

2. The tube is then heated by an external heater to a pre-defined temperature in this case a step of say 20°C to 40°C with no gas flow until the temperature remains stable at which point thermal equilibrium has been achieved.

3. A clean gas stream for example nitrogen is then used to flush the desorbed gases from the sorption tube to the sensor system which comprises an array of piezo-electric quartz crystal oscillated sensors for example and the response of the sensor system is recorded and stored.

The sequence of steps 2 and 3 above is repeated as appropriate either until a predefined number of steps have been carried out or until the sensor system can detect no further desorbed materials.

The recorded responses of the sensor system for each of the steps carried out is then treated with an appropriate data processing algorithm. In the current embodiment a standard technique, principal component analyses (PCA) is employed. This simply allows multi-dimensional data to be represented graphically in either two or three dimensions.

CLAIMS

1. A system for sensing chemicals, the system comprising
a sensor;
collecting means for collecting chemical species;
removal means for removing the species from the
collecting means and presenting them to the sensor; and
interpretation means for interpreting the information
obtained from the system.
2. A method for chemical sensing using a system
according to claim 1.
3. A system for obtaining chemicals from gaseous
liquid or solid samples, the system comprising:
a gas permeable means;
a chemically absorbent material;
sealing means for sealing the absorbent.
4. A system according to claim 1 or claim 3 further
comprising means for identifying a chemical sample.
5. A system according to claim 4, wherein the means
for identifying the sample comprises a bar code.
6. A system according to any one of claims 1, 3, 4 or
5, further comprising means for presenting samples to
analytical means for subsequent analysis.
7. A system according to any one of claims 1, 3, and
4 to 7, wherein the collecting means comprises means for
entrapping a chemical species.
8. A system according to claim 1, wherein the
interpretation means comprises a pattern recognition algorithm.

9. A system according to any one of claims 1 and 3 to 8, further comprising means for progressively removing either serially or in parallel the entrapped materials.

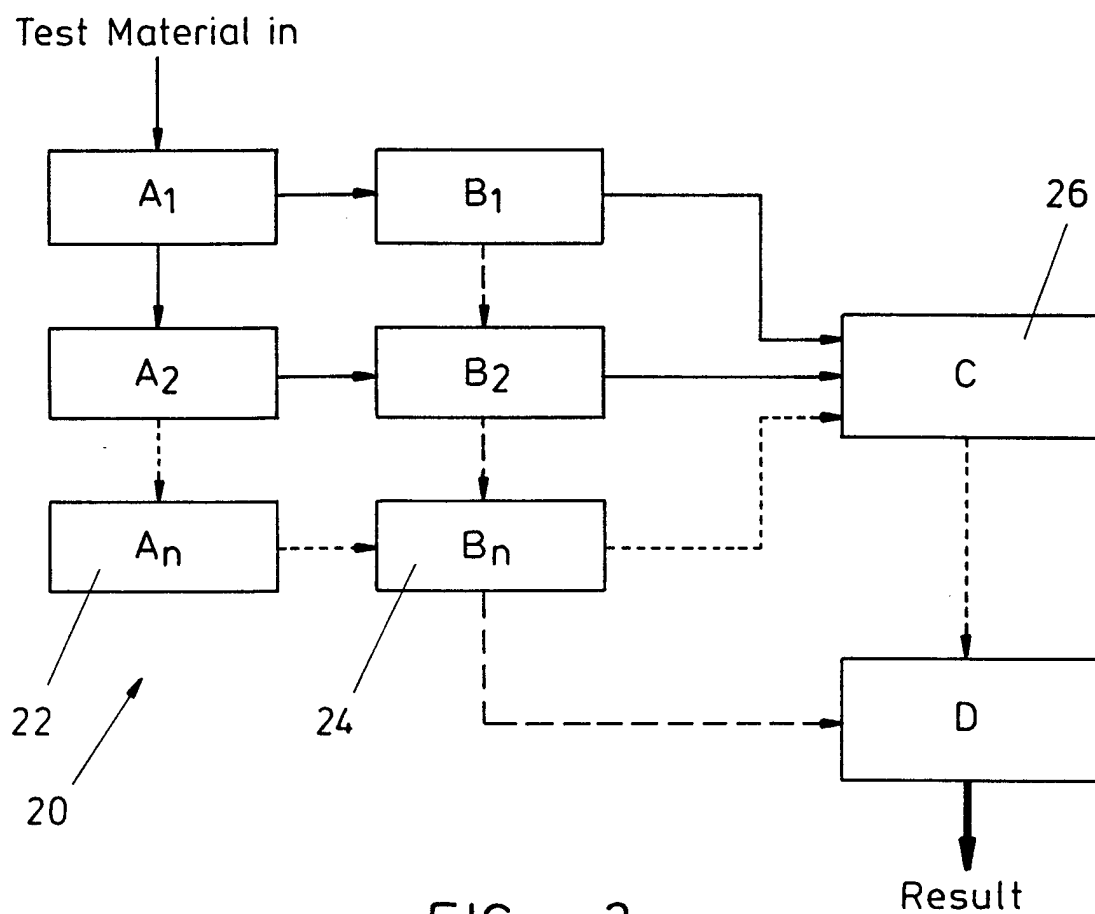
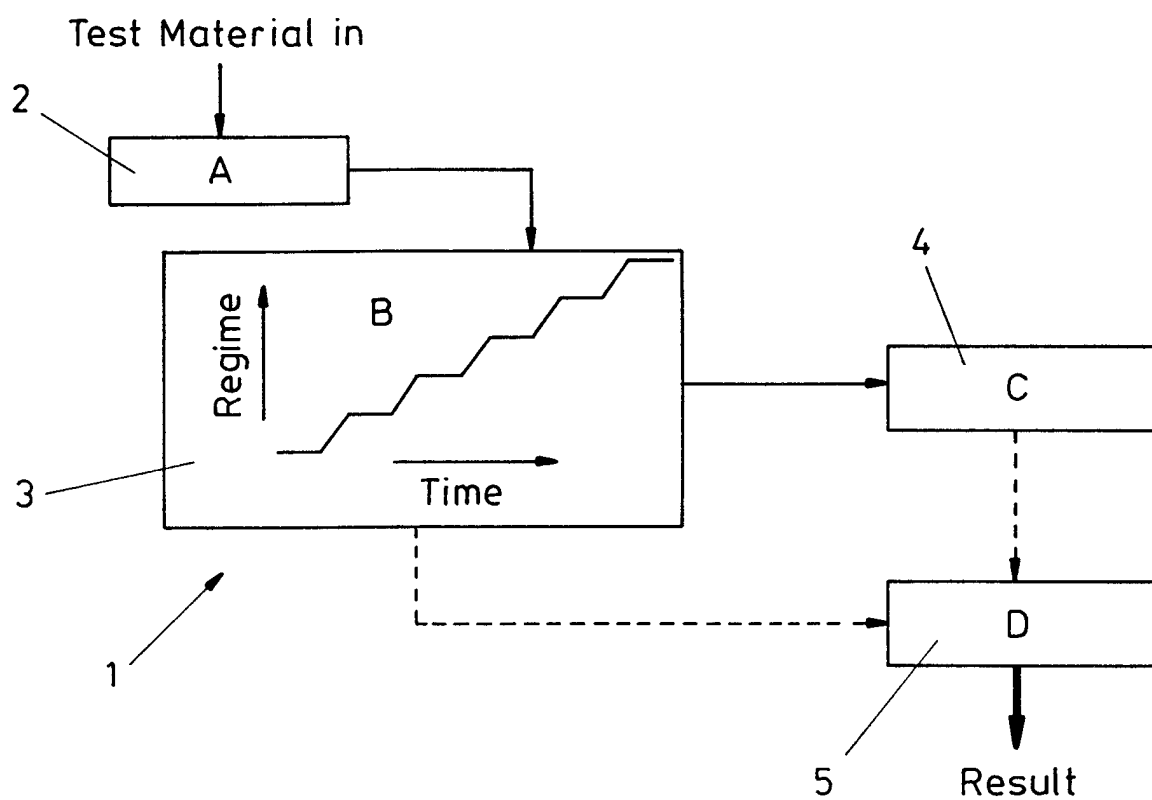
10. A system according to any one of claims 1 and 3 to 9, comprising a gas permeable membrane situated in a wall of a vessel, container or conduit.

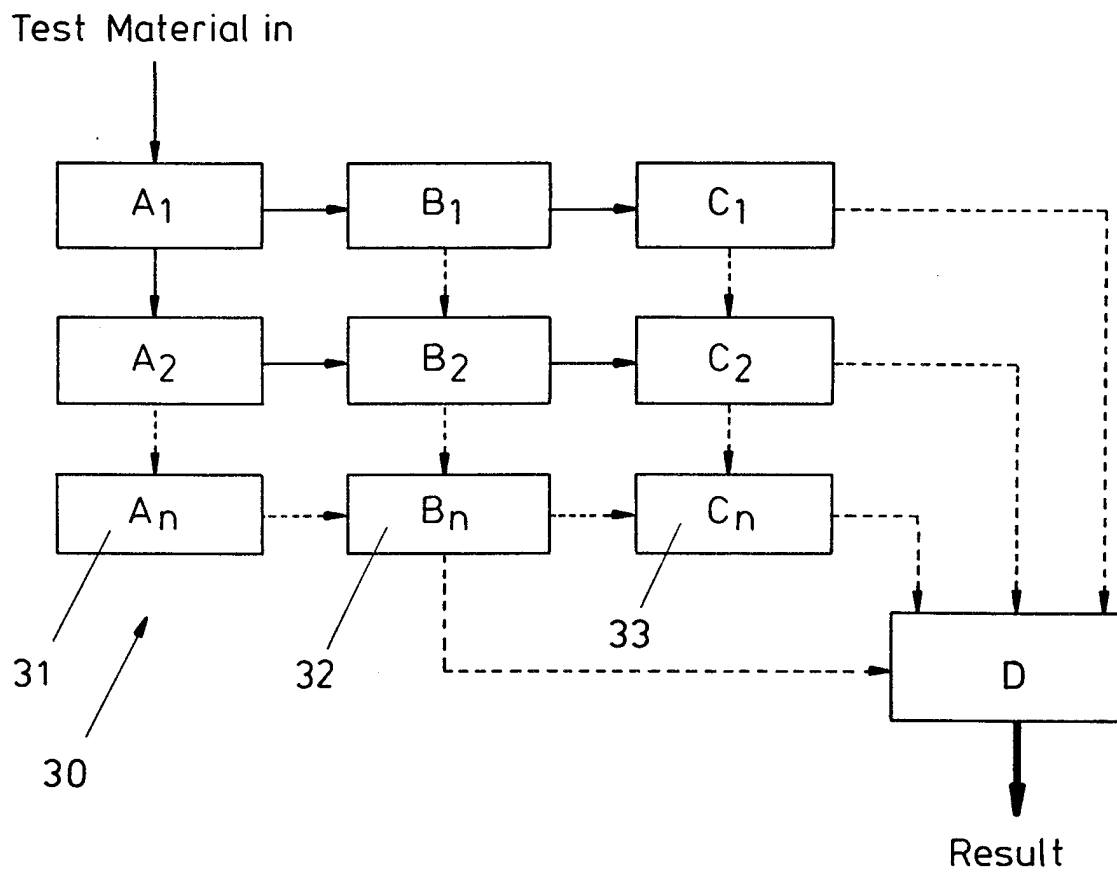
11. A system according to claim 10, wherein a gas permeable membrane has a pore size sufficiently small to retain bacteria.

12. A system according to claim 10 or claim 11, wherein the membrane further comprises a detector strip comprising a chemically absorbent material deposited on a gas impermeable backing matrix.

13. A system according to any one of claims 10 to 12, wherein the membrane further comprises a means to provide a gas-tight seal to the gas permeable membrane of a sample restrainer, and means to provide adhesion to the sample restrainer.

14. A system according to any one of claims 10 to 13, further comprising means to remove species in the absorbent material for subsequent presentation to analytical means.



FIG. 3

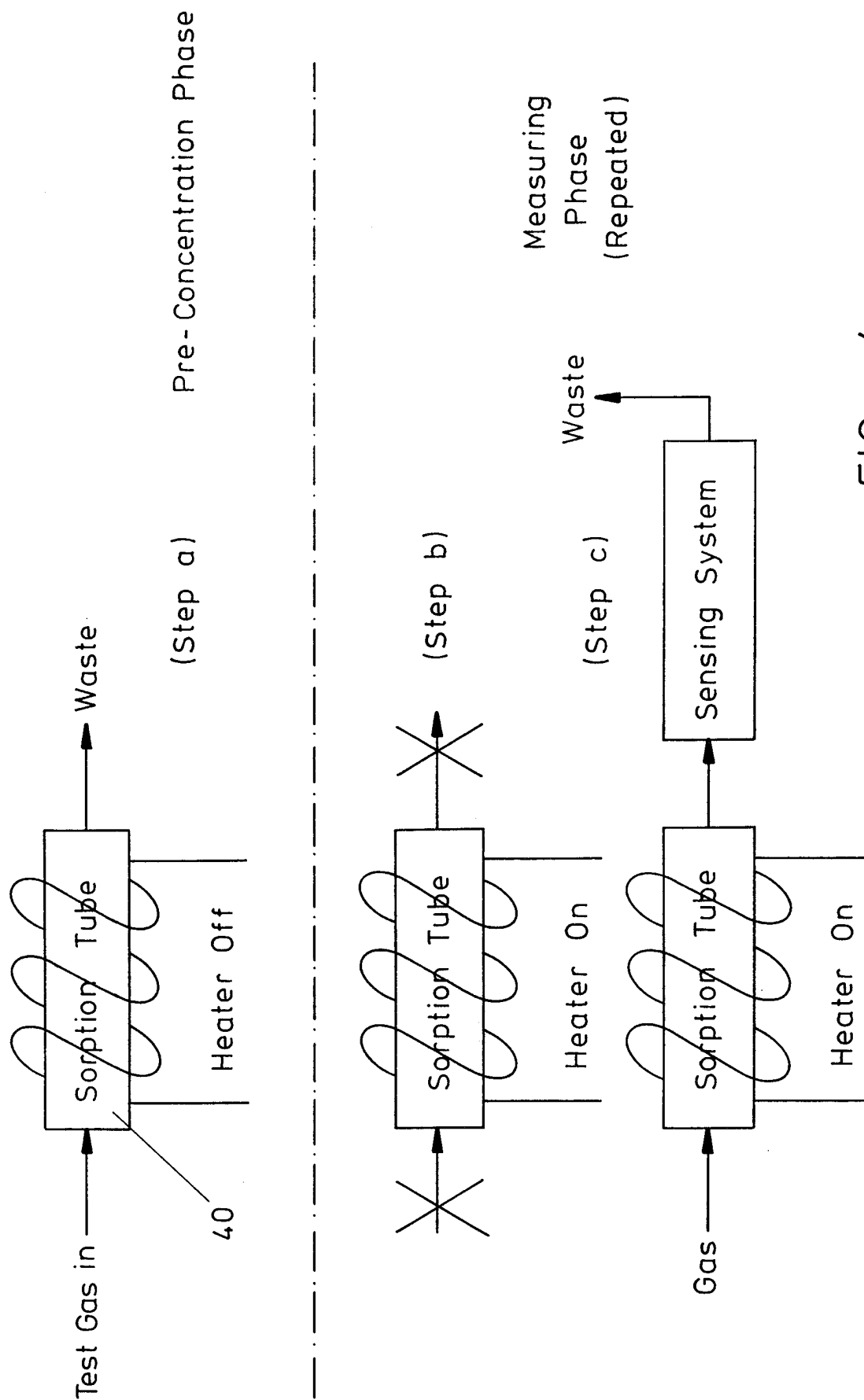
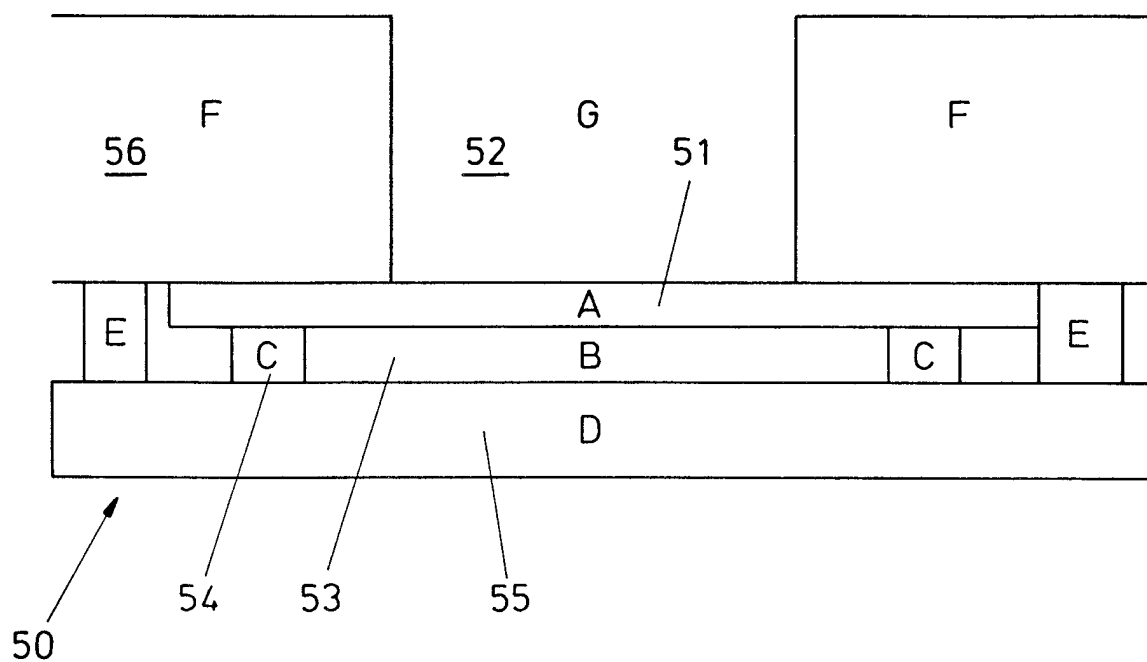
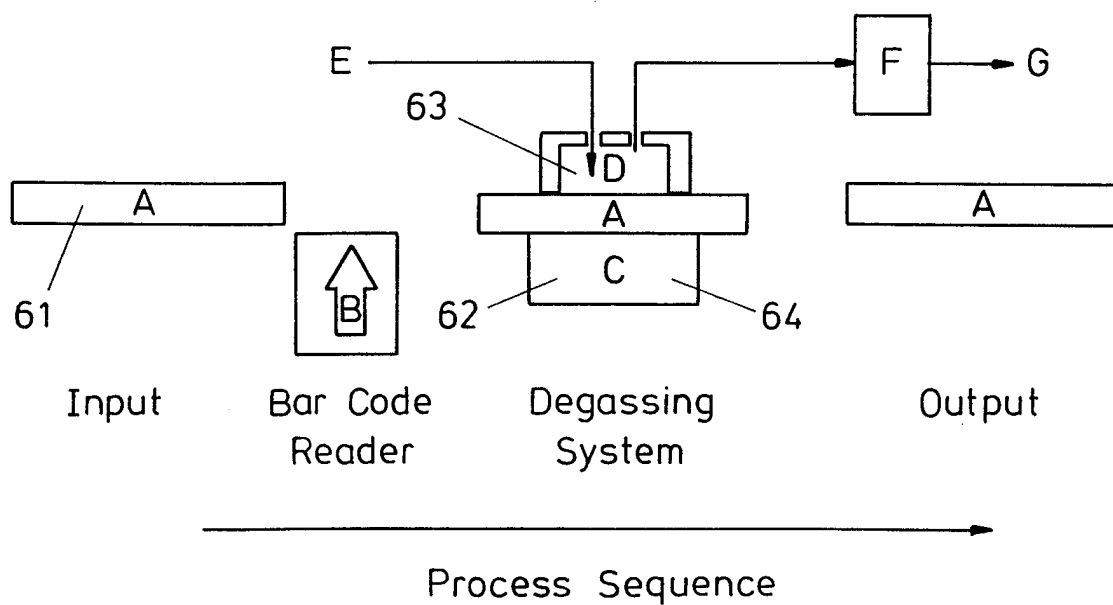


FIG. 4

FIG. 5FIG. 6

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 97/03100

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G01N1/22 G01N1/40

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)

IPC 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 980 294 A (ELIAS) 25 December 1990 see column 3, line 56 - column 4, line 2	1,2
Y	see figures	8
Y	US 5 469 369 A (ROSE-PEHRSSON) 21 November 1995 see abstract	8
X	US 4 327 575 A (LOCKER) 4 May 1982 see column 2, line 67 - column 3, line 32 see column 4, line 41 - line 50 see column 5, line 27 - line 45 see column 5, line 66 - column 6, line 14 see figures 1-4,8	3,4,6,7

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in 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.
X	US 4 040 805 A (NELMS) 9 August 1977 see column 2, line 53 - column 3, line 8	3,6,7
Y	see column 3, line 26 - line 46 see column 4, line 41 - last line	4,5
A	see figures ---	13,14
Y	US 5 549 819 A (NICKERSON) 27 August 1996 see column 1, paragraph 1 see column 8, paragraph 1	4,5
A	see column 11, line 22 - line 37 ---	1,3,6,7
A	GB 2 046 903 A (DU PONT DE NEMOURS) 19 November 1980 see page 1, line 56 - line 60 see page 2, line 12 - line 36 see page 3, line 11 - line 13 see figures 1,2 ---	1,3,12
A	GB 2 250 633 A (EXTREL) 10 June 1992 see page 29, line 6 - line 18; figure 1A -----	9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 97/03100

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4980294 A	25-12-90	NONE	
US 5469369 A	21-11-95	NONE	
US 4327575 A	04-05-82	NONE	
US 4040805 A	09-08-77	CA 1104043 A DE 2736975 A GB 1555856 A JP 53053396 A	30-06-81 27-04-78 14-11-79 15-05-78
US 5549819 A	27-08-96	US 5716525 A	10-02-98
GB 2046903 A	19-11-80	US 4235097 A AR 221141 A AU 519777 B AU 5686780 A BE 882442 A BR 8001685 A CA 1133326 A DE 3011908 A FR 2452702 A JP 1345323 C JP 55140182 A JP 61011386 B NL 8001775 A SE 8002335 A	25-11-80 30-12-80 24-12-81 09-10-80 26-09-80 18-11-80 12-10-82 09-10-80 24-10-80 29-10-86 01-11-80 02-04-86 30-09-80 28-09-80
GB 2250633 A	10-06-92	JP 4274728 A US 5142143 A	30-09-92 25-08-92