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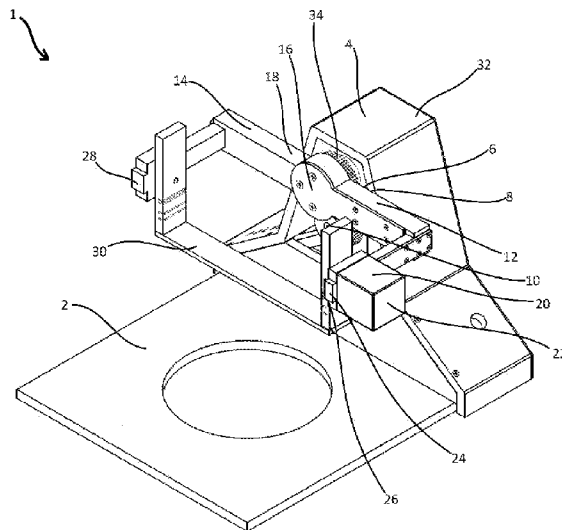


FIG. 1

(57) Abstract: A multi-axis reactor including a base having a support extending upwardly from the base, a first motor having a stator fixedly connected to the support, the rotor axis of rotation being horizontally oriented, an arm operatively connected to the first motor's drive shaft, the arm extending radially outwardly from the first motor's drive shaft, a second motor having a stator fixedly connected to an end of the arm, the rotor axis of rotation being parallel to the arm, a closable vessel being fixedly connectable to the second motor's drive shaft, each of the first and second motors being operatively connectable to a processor-based control system, and each of the first and second motors being actuatable by control system machine-readable code containing a set of instructions such that upon rotation of the motors the contents of the vessel are subjected to a modified gravity environment.

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A MULTI-AXIS REACTOR AND METHOD

The present invention relates to reactors and in particular to bioreactors and methods for their use.

The invention has been developed primarily as a bioreactor and method for producing cells, bacteria, and their by-product and will be described herein with reference to this application. However, it will be appreciated that the invention is not limited to this particular field.

BACKGROUND OF THE INVENTION

Any discussion of prior art throughout the specification should in no way be considered as an admission that such prior art is widely known or forms part of the common general knowledge in the field.

A bioreactor is a device, apparatus or system designed for production processes that effect and support the growth of biological organisms and biochemical reactions under controlled conditions. Bioreactors are used in a variety of fields and industries, including biochemistry, microbiology, biotechnology, and chemical engineering.

A bioreactor typically consists of a container or vessel within which a biological system or (i.e., sample) is housed, and the biochemical reactions take place. The vessel is designed to be sterile to prevent contamination of the biological system and is often made from stainless steel or glass.

The vessel also includes mechanical components to enhance biological growth and biochemical reactivity such as an agitator, which is used to mix the contents of the vessel and provide oxygen to organisms. The agitator can be designed as a mechanical impeller or a magnetic stirrer, which can be controlled to provide different mixing rates to ensure that nutrients and gases are evenly distributed throughout the vessel and its contents. In some type of bioreactors, the contents can be mixed by shaking or rotating the vessel, such as in a dual-axis bioreactor.

A bioreactor may have a temperature control system designed to maintain a constant temperature within the vessel. This is achieved using heating and cooling systems, which can be controlled to provide the necessary temperature range for the biological system.

A bioreactor may have a system for controlling the pH level of the biological system. This is typically achieved using buffers or chemicals that can be added to the vessel to maintain a stable pH level.

Finally, a bioreactor might also have a system for monitoring and controlling the oxygen and nutrient levels within the vessel. This can be achieved by sensors that measure the levels of dissolved oxygen and nutrients and can be used to adjust the agitator and other mechanical components to ensure optimal growth conditions.

Dual-axis bioreactors are a type of bioreactor that typically provides both mixing and gas transfer in a single vessel. They are also known as orbitally shaken bioreactors and are commonly used for microbial fermentation and cell culture applications.

In a dual-axis bioreactor, the vessel is mounted on a platform that rotates on two axes simultaneously. This creates a random, three-dimensional movement of the culture, which provides efficient mixing and aeration. The platform is typically driven by a motor.

In a production process, known bioreactors produce limited quantities of only a few types of biological organisms such as cells, pre-cursor cells, and bacteria. Known bioreactors produce by-product in limited quantities.

AN OBJECT OF THE INVENTION

It is an object of the invention to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

It is an object of the invention in its preferred form to provide a bioreactor and method that can produce many types of biological organisms or by-product and can produce greater quantities of one of these during a production process.

SUMMARY OF THE INVENTION

According to the invention there is provided a multi-axis reactor including:

- a base having a support extending upwardly from the base;

a first motor having a stator fixedly connected to the support, the rotor axis of rotation being horizontally oriented;

an arm fixedly connected to the first motor's drive shaft, the arm extending radially outwardly from the first motor's drive shaft;

a second motor having a stator fixedly connected to an end of the arm, the rotor axis of rotation being parallel to the arm;

a closable vessel being fixedly connectable to the second motor's drive shaft;

each of the first and second motors being operatively connectable to a processor-based control system; and

each of the first and second motors being actuatable by control system machine-readable code containing a set of instructions such that upon rotation of the motors the contents of the vessel are subjected to a modified gravity environment.

The set of instructions preferably further include instructions to rotate each of the first and second motor at 11 rotations per minute.

A second arm preferably extends radially outwardly from the first motors' draft shaft and into the opposite direction of the first arm, the end of the second arm being rotatably connectable to a vessel at a location coaxial to the second motor's drive shaft.

Preferably, there is further included a gear system operatively connecting the first motor to the arm.

There is preferably further included a gear system operatively connecting the second motor to the closable vessel.

Preferably, the gear system has a 1:1 gear ratio.

The first and second arm preferably form a bracket.

According to another aspect of the invention there is provided a method for processing biomaterials including the steps of:

preparing one or more biomaterials for processing in a multi-axis reactor;

depositing the one or more biomaterials into the reactor vessel;

securely closing the vessel; and

rotating each of the first and second motors of the multi-axis reactor, the motors being rotated at 11 rotations per minute for a predetermined period.

BRIEF DESCRIPTION OF THE DRAWINGS

A preferred embodiment of the invention will now be described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 is an isometric perspective view drawing of the multi-axis reactor according to the invention;

Figure 2 is a front view drawing of the multi-axis reactor according to the invention;

Figure 3 is a side view drawing of the multi-axis reactor according to the invention; and

Figure 4 is a top view drawing of the multi-axis reactor according to the invention.

PREFERRED EMBODIMENT OF THE INVENTION

Referring to the drawings, the multi-axis reactor 1 (i.e., bioreactor) has a base 2 with a support 4 extending upwardly from the base 2. A first motor's 6 stator 8 is fixedly connected to the support 4 such that the first motor's rotor 10 axis of rotation (not shown) is oriented horizontally relative a reference ground (not shown) plane on which the base 2 is positioned. First and second arms 12 and 14 are each fixedly connected to the first motor's drive shaft 16, each arm 12 and 14 extending radially outwardly in an opposite direction to that of the other arm 12 and 14. Together, the arms 12 and 14 form a bracket 18 fixedly connected to the first motor's drive shaft 16 at an intermediate location along the bracket 18.

The stator 20 of a second motor 22 is fixedly connected to an end 24 of the bracket 18 such that the rotor axis of rotation (not shown) is in parallel to the bracket 18 along the length of the bracket 18. One end of a closable container (not shown), in the form of a biological sample container, is fixedly attachable to the second motor's 22 drive shaft 26. The other end of the closable container is rotatably connected to the other end 28 of the bracket 18 at a location coaxial to the second motor's drive shaft 26.

In a preferred embodiment shown in Figure 1, a second bracket 30 is connected to the second motor's drive shaft 26 at one end and rotatably connected to an end 28 of the first bracket 18 at the second bracket's other end, coaxial to the second motor's drive shaft 26. The biological sample container (not shown) is fixedly attachable (or i.e., connectable) to the second bracket 30. As shown in Figure 1, a 1:1 gear system 34 operatively connects the first motor 6 to the bracket 18.

In a preferred embodiment, the bracket 18 is directly connected to the first motor's drive shaft 16.

In a preferred embodiment, each gear system 34 includes a corresponding two gears.

In a preferred embodiment, a container holder (not shown) in the form of a bracket is fixedly connectable to the bracket 18 by means of one more slot arrangement (not labelled).

Each of the first and second motors 6 and 22 are operatively connected by means of suitable power electronics circuits and wiring to a processor-based control system in the form of a microcontroller 23 storing a control system having machine-readable set of instructions adapted to rotate each of the motors at 11 rotations per minute such that the contents of the container are subjected to a modified gravity environment 10^{-3} G (not shown).

The various physical parts of the multi-axis reactor 1 are made from plastic, but can be made from metal, rubber, or other suitable material, and are connected by means of fasteners (not labelled) in the form of bolts, but can be glued together, 3-D printed, screwed together, etc.

In preferred embodiment, the microcontroller 32 is interfaced to a USB and one or all of the machine-readable set of instructions are provided to the microcontroller 32 by a processor-based system using USB or another suitable computer communication method such as LAN or Wi-fi.

In a preferred embodiment, the multi-axis bioreactor 1 is without a microcontroller 32 but is connectable to a microcontroller.

In a preferred embodiment, there the multi-axis bioreactor 1 has UI for controlling motor RPM and actuation duration.

The motors 6 and 22 can be selected to be any suitable motors capable of performing the invention.

The gear ratio can be selected to be any suitable gear ratio capable of performing the invention.

The microgravity G values can be another suitable value.

In a preferred embodiment, the multi-axis reactor further includes one or more of a temperature sensor, a moisture sensor, colour, gas, IR, and a gravity sensor operatively connected to the microcontroller 32 and at a suitable location to the biological sample container (not shown) such that its contents can be measured. Data obtained from reaction processes operated by means of the multi-axis reactor is used to train a Neural Network model (not shown) adapted to optimise the reaction process by controlling the RPM of each of the motors 6 and 22, and hence the overall G the content of container is subjected to. This can be achieved by using Neural Network training techniques that include preparing the sensor data, building a model, training the model, and updating the model's performance such that the model is able to optimise the reaction process to a target level, or other suitable Artificial Intelligence techniques such as Reinforcement Learning.

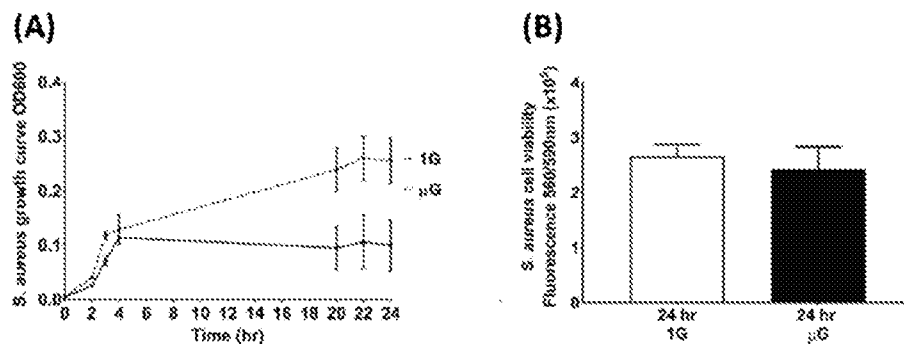
The Person Skilled in the Art ("PSA") will appreciate that in a preferred embodiment the multi-axis reactor 1 is an embedded system. Embedded systems typically include hardware in the form of a microprocessor or microcontroller 32 interfaced with sensors and actuators by means of a printed circuit board. Software stored in system memory executes machine-readable code containing a set of instructions for operating the embedded system.

The PSA will appreciate that a biological sample container is a known type of container that uses comprises flasks and/or tubes for storing one or more corresponding biological sample.

To process and produce (i.e., culture, grow etc.) biomaterials using the multi-axis reactor 1 in a production process, a user firstly prepares a target biomaterial, e.g. *S. aureus*, for processing in the multi-axis reactor by culturing a requisite amount of the *S. aureus* (not shown). The *S. aureus* is mixed with approximately 150 and 250mL of culture medium wherein there is approximately 60% to 70% confluency and then deposited into a one or more 25cm² to 75cm² flask or tube of the closable vessel in the form of a standard biological sample container (not shown). The container is then securely closed.

Next, the multi-axis reactor 1 is powered on. The microcontroller 32 executes the control system machine-readable code containing the set instructions causing the motors 6 and 22 to each rotate at 11 RPM to thus cause container (not shown) to rotate on its x and y axes by means of the brackets 18 and 30 such that the *S. aureus* inside the container is subjected to a modified gravity environment 10^{-3} G process for a suitable period of time sufficient for the *S. aureus* to react and produce an increase in the amount of *S. aureus* to a target parameter. In a preferred embodiment, a trained Neural Network controls the RPM based on sensors data received from within and/or outside of the container.

The PSA may refer to the following exemplary results charts A and B, depicting *S. aureus* growth as grown in the multi-axis reactor according to the invention:



Charts A and B depicting *S. aureus* growth and cell viability

The PSA will appreciate that best results are produced closer to the point of intersection of the x and y axes of rotation of the container.

The PSA will appreciate that the multi-axis bioreactor 1 and corresponding method can be used to produce growth of human and other mammalian cells, as well as bacterial cells, viruses, fungi, and tissue-like three-dimensional cell constructs (not shown).

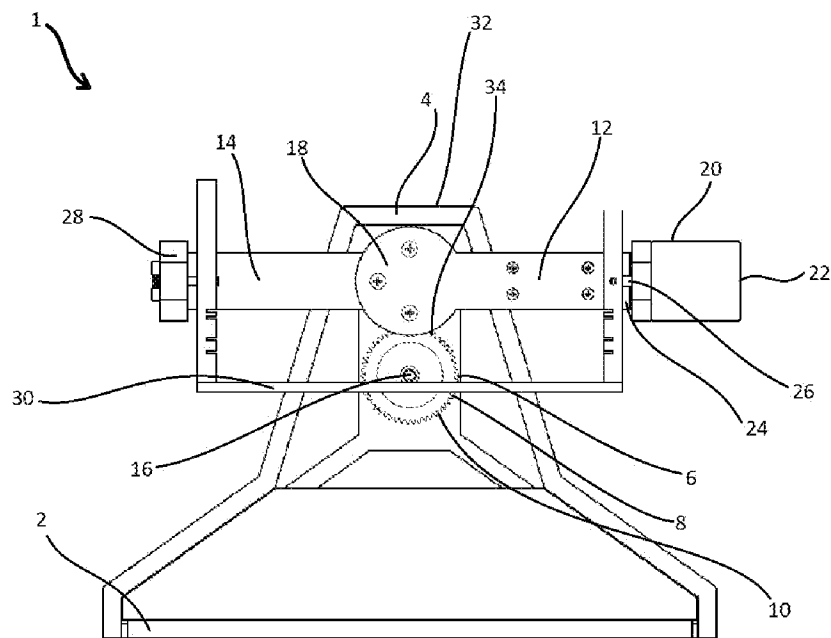
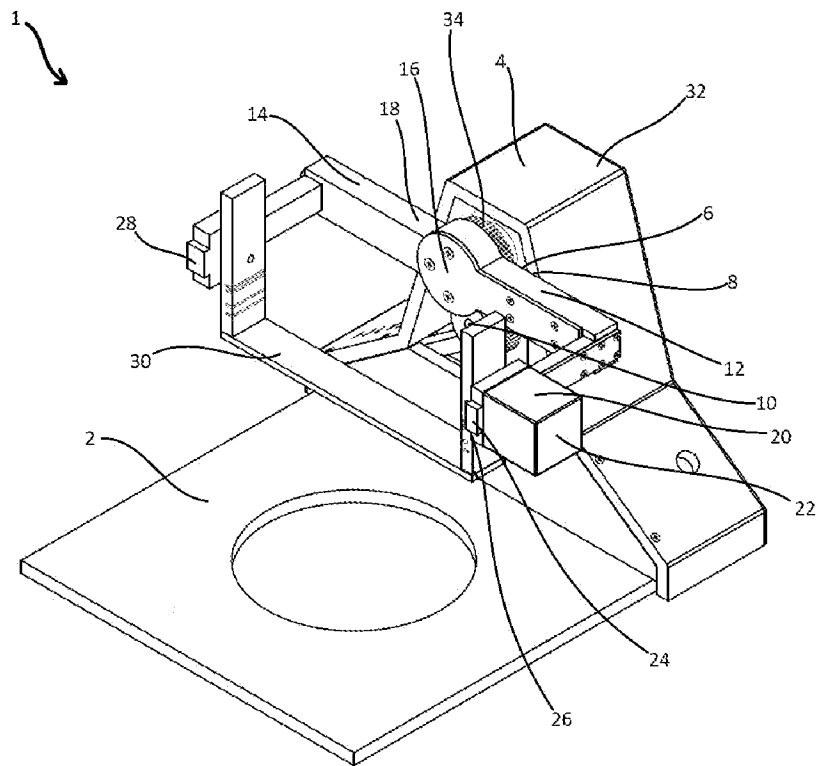
In a preferred embodiment, a plurality of biomaterials (not shown) can be processed at once by the multi-axis reactor.

It will be appreciated that the illustrated multi-axis reactor and method can produce many types of biological organisms or by-product and can produce greater amounts of one of these during a production process.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A multi-axis reactor including:
 - a base having a support extending upwardly from the base;
 - a first motor having a stator fixedly connected to the support, the rotor axis of rotation being horizontally oriented;
 - an arm operatively connected to the first motor's drive shaft, the arm extending radially outwardly from the first motor's drive shaft;
 - a second motor having a stator fixedly connected to an end of the arm, the rotor axis of rotation being parallel to the arm;
 - a closable vessel being fixedly connectable to the second motor's drive shaft;
 - each of the first and second motors being operatively connectable to a processor-based control system; and
 - each of the first and second motors being actuatable by control system machine-readable code containing a set of instructions such that upon rotation of the motors the contents of the vessel are subjected to a modified gravity environment.
2. A multi-axis reactor according to claim 1, the set of instructions further including instructions to rotate each of the first and second motor at 11 rotations per minute.
3. A multi-axis reactor according to claim 1 or claim 2, further including a second arm extending radially outwardly from the first motors' draft shaft and into the opposite direction of the first arm, the end of the second arm being rotatably connectable to a vessel at a location coaxial to the second motor's drive shaft.
4. A multi-axis bioreactor according to any one of claims 1 to 3, further including a gear system operatively connecting the first motor to the arm.
5. A multi-axis reactor according any one of claims 1 to 4, further including a gear system operatively connecting the second motor to the closable vessel.
6. A multi-axis reactor according to claim 4 or 5, wherein the gear system has a 1:1 gear ratio.

7. A multi-axis reactor according to any one of claims 1 to 6, wherein the first and second arm form a bracket.
8. A method for processing biomaterials including the steps of:
 - preparing one or more biomaterials for processing in a multi-axis reactor;
 - depositing the one or more biomaterials into the reactor vessel;
 - securely closing the vessel; and
 - rotating each of the first and second motors of the multi-axis reactor, the motors being rotated at 11 rotations per minute for a predetermined period.



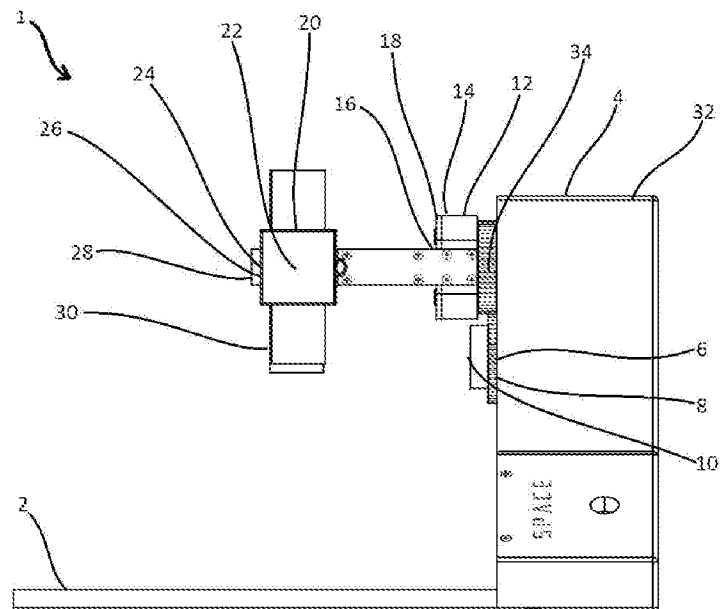


FIG. 3

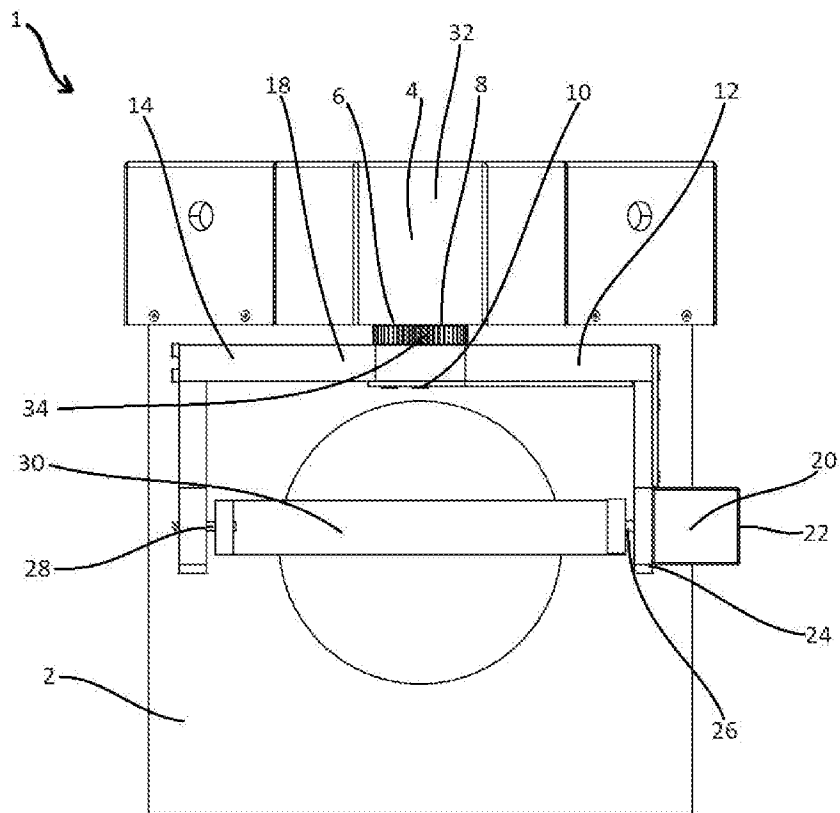


FIG. 4

A. CLASSIFICATION OF SUBJECT MATTER

C12M 3/06 (2006.01) C12M 1/34 (2006.01) C12M 3/00 (2006.01)

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)

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)

PATENW cluster (EPODOC, TXTE Cluster), WPIAP; CPC/IPC as appropriate: C12M1/00, C12M1/10, C12M21/00, C12M27/10, C12M27/14, C12M27/16, C12M41/42, B01F31/00, B01F29/00. Classification used in various combinations and with selected keywords: clinostat, biaxial, rotor, rotary, reactor, drum, cell culture, motor, control, program, speed, drive, spin, revolve, gravity and similar terms. Applicant and inventor names searched in IP Australia internal databases.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	



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 "D" document cited by the applicant in the international application "E" earlier application or patent 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		"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 "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 "&" document member of the same patent family
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Date of the actual completion of the international search 11 July 2024	Date of mailing of the international search report 11 July 2024
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustalia.gov.au	Authorised officer Catriona Condon AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. +61 2 6283 2326

INTERNATIONAL SEARCH REPORT		International application No.
C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		PCT/AU2024/050555
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	US 2003/0041800 A1 (UEMURA et al.) 06 March 2003 Figs. 1, 11; [0048, 0052-0056].	1-8
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Form PCT/ISA/210 (fifth sheet) (July 2019)

INTERNATIONAL SEARCH REPORT		International application No.	
Information on patent family members		PCT/AU2024/050555	
This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.			
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		WO 2014200084 A1	18 Dec 2014
End of Annex			
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.			