DESKTOP RPM: NEW SMALL SIZE MICROGRAVITY SIMULATOR FOR THE BIOSCIENCE LABORATORY

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ABSTRACT

A small size 'Random Positioning Machine' (RPM) is described that will enable simulation of microgravity in the bioscience laboratory. The so-called Desktop RPM contains two perpendicular cardanic frames, with an experiment platform, that are moved according to a 'random walk scenario' generated by software in a PC. Electrical interface to experiment packages mounted on the experiment platform is provided by means of 12 channels that are routed over slip-ring capsules. The control scenario keeps the walk speed constant at a pre-selected value and rejects walk speed direction changes that would generate accelerations above a pre-selected threshold. The instrument is intended to be operated inside an incubator that will provide control of temperature and atmospheric composition to the experiment (%CO_2, rH, etc.). Standard consumable experiment hardware can be used. More sophisticated hardware, derived from spaceflight experience, will enable automatic medium exchange, fixation, etc. The instrument, its control software and various types of automated experiment hardware can be provided by Fokker Space at attractive recurring cost and delivery time. Primary application areas foreseen at present are cell and developmental biology and tissue engineering.

Keywords: *microgravity simulation, bioscience research, cell biology, developmental biology, tissue engineering*

1. INTRODUCTION

Microgravity simulation in bioscience research by means of 3d continuous or (quasi-)random rotation around the direction of gravity is used at least since 1963 (Ref. 1) and was pioneered especially by dr. Hoson in Japan (Refs 2, 3). In 1994 the notion of 'true random positioning' was advocated by dr. D. Mesland, then at the European Space Agency, and a contract for the development of a prototype instrument was awarded to Fokker Space (Ref. 4). The prototype 'Random Positioning Machine' (RPM) eventually entered service at the Dutch Experiment Support Center (DESC) in Amsterdam in 1997 (Ref. 5). Two more RPMs were delivered to the Space Biology Group at the ETH-Zürich (1998; Ref. 6) and to the University of Sassari (Sardinia, Italy; 1999). This first series of instruments is capable of carrying appreciable experiment packages, e.g. such as required in research on extended objects (plants, animals, etc.) and which may include conditioning (e.g. a thermostat) and diagnostics (sensor packages, microscope, video equipment, etc.). Soon, however, also the interest in more moderately sized RPMs was noticed. An in-house project at Fokker Space was initiated in January 2000 and the Desktop RPM prototype presented in this paper was conceived. After a careful review of the design, and finalization of the sophisticated control software, the instrument is now commercially available for much less cost compared to the 'classical' RPM.

2. PRINCIPLE

Microgravity simulation by means of continuous random change of orientation of objects relative to the gravity's vector can generate effects comparable to the effects of true microgravity when the changes are faster than the object's response time to gravity. Thus, slow responsive living objects, like plants, are excellent candidates to be studied on RPMs. The random 'angular walk speed' (ω; rad/s) can be low and the unavoidable spurious centrifugal weight encountered by objects at radius R out of the center of rotation and with (effective) mass M will remain also low (=$M\omega^2R$), indeed allowing for extended objects.

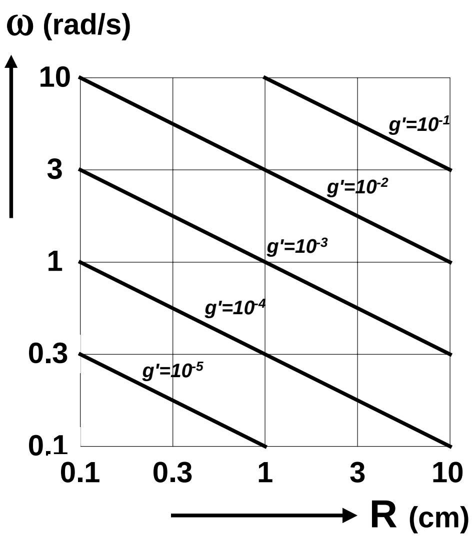

Figure 1
Quick-look 'equi-g' contour' plot

For fast responsive passengers, the quick-look log(R)-log(ω) plot presented in Figure 1 can be used to match required 'angular walk speed' with culture size. When using e.g. an 2d-array, or 3d-stack, of different cultures accommodated in multiwell plates, it is easy to read-off 'equi-g'-contours' (i.e., circles or spheres, respectively, where $g'=\omega^2 R/g_0$ with $g_0=9.81$ m/s² being the Earth's gravitational acceleration) around the center of rotation, corresponding to the selected (or necessary) value of ω. As an example: when fast weight response requires a random rotation with ω=1 rad/s, and microgravity simulation should remain below $g'=10^{-3}$, the diameter of the object or culture must be kept smaller than 2xR=2 cm.

Figure 1 shows that a realistic operational region is centered around 'some' rad/s for ω and 'some' centimeters for R. This has led to the values adopted in the design of the desktop RPM instrument presented here.

In order to effectively use the 'quick-look' assessment presented in the above, it is important that the angular 'walk speed' ω is kept constant. Indeed, this has been the major design driver for the sophisticated control software developed for the desktop RPM. The value of ω can be selected from a menu in the PC user interface before starting the experiment run.

The remaining source of spurious weight is, of course, change in walk speed direction. As a first approximation it may be argued that this weight is offered in random directions and may average out. Nevertheless, and especially to avoid accumulation effects, the desktop RPM software operates in two steps in order to be able to minimize this effect. In the first step a random 'constant ω walk path' of selected length (=duration) is generated, in which (random) 'walk direction' changes that exceed a certain pre-selected criterion are rejected. This criterion is expressed at the user interface in degrees for easy reference. In the second step this path is 'walked' by the instrument's frames. Meanwhile, a new approved path can be generated that can be linked smoothly to the previous path by starting at the end point and keeping the direction-change criterion invoked. Walk path files are generated and stored in the PC and these may be 'walked again' when desired.

3. DESCRIPTION OF THE SYTEM AND OF THE INSTRUMENT

A schematic system overview is presented in Figure 2. The system consists of a PC, a 'Dual Motor Controller' (DMC) and the instrument. The PC acts as user interface and executes the control software. The DMC is the interface between PC and the instrument. A small box containes its microprocessor-based electronics that command the motors and read-out the corresponding encoders. The DMC is connected to the PC's RS232 com port and to the pertinent connector on the instrument. The DMC is fed directly from mains.

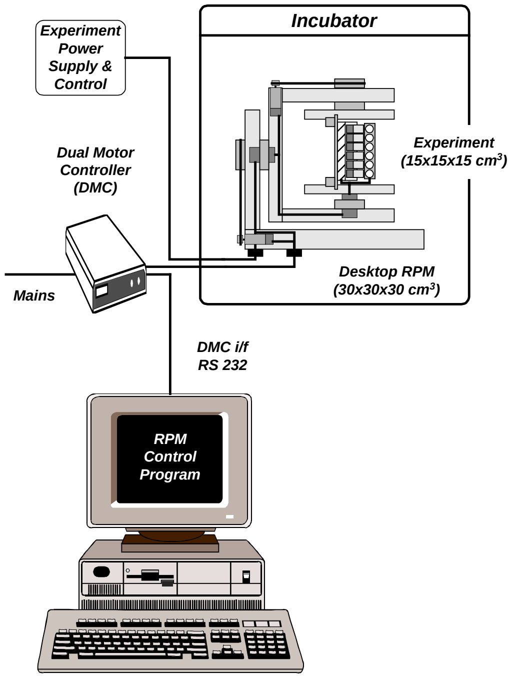

Figure 2
Desktop RPM System Diagram

The actual instrument is sized to fit inside an incubator that should allow feed-through of the cable from the DMC. Selection of materials and components was made subject to the corresponding environmental requirements.

Figure 3
Desktop RPM prototype instrument 'front view'

A picture of the prototype instrument is given in Figure 3. Specifications are summarized in section 4. The instrument consists of a sturdy base-frame and two cardanic frames. The base-frame stands on rubber feet that are adjustable in height (range 4 mm) and on which all interface connectors are mounted.

The outer cardanic 'U-shaped' frame is mounted on the base-frame by means of one single circular bearing in which an 18-tracks slip-ring capsule is accommodated (Figure 4). This frame is driven by a DC electro-motor with gearbox and encoder, mounted on the base-frame. The transmission is formed by a two tooth-wheels, a tooth- belt and a spanner wheel. The motor with gearbox and encoder for the inner frame is mounted inside the outer frame structure and electrical connection is made over 6 of the 18 slip-ring tracks.

The inner frame consists of two side-bars, connected by the experiment platform. This frame is mounted by means of two circular bearings in the 'U-shaped' outer frame and one of these bearings holds the second 18-tracks slip-ring capsule in the instrument. Twelve channels are routed from the experiment platform, over both slip-ring capsules, to a connector on the base-frame. The belt drive of the inner frame at the other bearing is analogous to that of the outer frame.

The experiment platform can be mounted at 5 different levels in the inner frame (13 mm steps) so as to locate the center of the experiment specimen in the center of rotation. Two balance masses in the inner frame's sidebars can be shifted and fixed in position to compensate for unbalance caused by the experiment platform and its passenger package. Velcro straps are used to tie platform and package together.

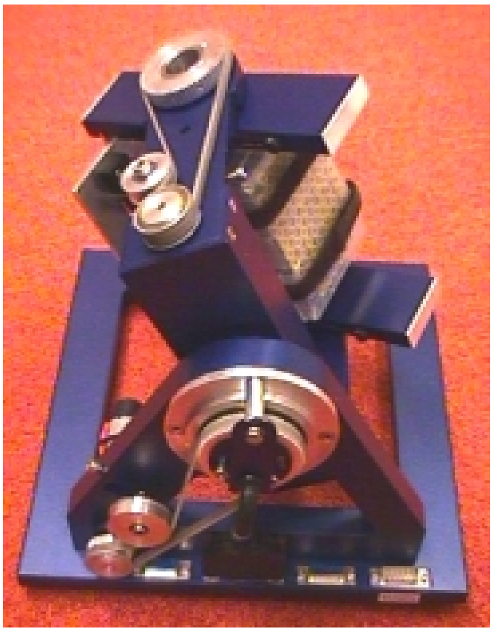

Figure 4
Desktop RPM prototype instrument 'rear view'

4. SPECIFICATIONS OVERVIEW

The specifications of the desktop RPM system and instrument are summarized in the table below.

System Element	Specification
PC	• Pentium-type with free RS232 com port • Windows 95, 98 • RS232 interface cable • desktop RPM software with user interface
DMC	• Motcon Lite with embedded software*) in box with mains on/off and 'reset' switches • DMC cable with 15 pins subD connectors
desktop RPM instrument	• Size: 30x30x30 cm^3 • Mass: 7.0 kg • Materials: coated aluminum and stainless steel • 15 pin female subD connector on chassis for DMC cable • Experiment volume: 15x15x15 cm^3 (max) • Experiment mass: 1.5 kg (max) • 12 slip-ring tracks available to experiment platform via15 pin male subD connector on chassis • Motors/gear boxes: Maxon 110212/110396 • Encoders: Maxon 110521 • Slip-ring capsules: Litton AC 6023-18 • Random walk 'speed' range: $0.1 < \omega < 3$ rad/s

*) 'Motcon Lite' is a Fokker Space in-house product

5. ON APPLICATIONS AND EXPERIMENT HARDWARE

The experiment hardware shown, as an example, in Figures 3 and 4 consists of commercially available pipette tip arrays and boxes, each tip closed by its usual rubber stop. These arrays are available with many different tip sizes and may suit a wide variety of experiments. Other experiment configurations may consist of commercial multiwell plates, suitably covered with foil to avoid spillage of liquids (e.g., Ref.

7). More sophisticated experiment hardware may offer quick and easy and/or in-run automated liquid handling (medium refreshment, fixation) and gas-exchange with the incubator's ambient.

One path studied at Fokker Space is to provide multiwell plates with individual or arrays of 'plugs'. These plugs have replaceable septa to flush medium by means of needles & syringes and offer a hydrophobic filter port for gas exchange. A prototype 19x19 mm^2 multiwell plug is pictured in Figure 5.

Figure 5
RPM multiwell plug prototype

The re-usable plug is composed of biocompatible and fully autoclavable materials (polysulphone, stainless steel) and consumable items (silicone rubber septa, hydrophobic filter). Testing and evaluation of this plug concept is being performed. Still, the major obstacle in this concept is that the 'random walk' has to be stopped to allow access to the plugs. Although procedures can be optimized, an automated system could be preferable in some cases.

Automated experiments on an RPM resemble true spaceflight experiments in many senses. During the last few years, Fokker Space has invested efforts to arrive at a collection of re-usable and automated experiment hardware concepts that can be arranged in various configurations to meet different experiment requirements.

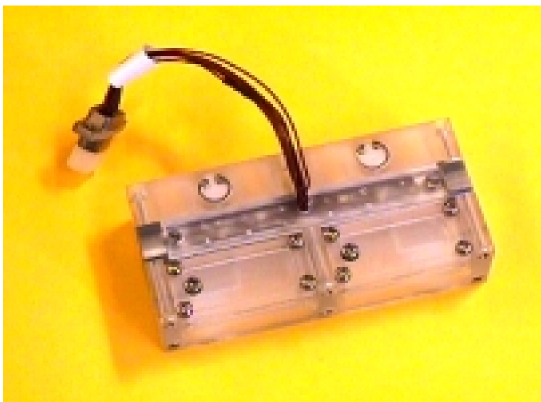

Figure 6
LIDIA-2 Experiment Unit for attached cells

As an example, modular so-called LIDIA units have been developed (=Liquid Dispenser Assemblies; size 2x4x8 cm^3) that are completely re-usable, have been tested for biocompatibility and operational reliability and will be used on a sounding rocket mission in November 2001.

Use of the LIDIA-2 unit (Fig. 6) is aimed at attached cells. The unit has two independent culture compartments, each served by two liquid storage chambers (e.g., activation, fixation). Gas exchange hatches for the culture compartment are available. The LIDIA-3 unit (Fig. 7) is intended for cells in suspension and its operation is based on the use of filters and motorized syringe pistons. Two culture compartments can be activated and fixed simultaneously from two liquid storage chambers. For more details see Ref. 8. Technology used in these units is considered mature. Both the LIDIA units or other assemblies based on this technology, like combinations of re-usable LIDIA parts with disposable multiwells, can be manufactured recurrently.

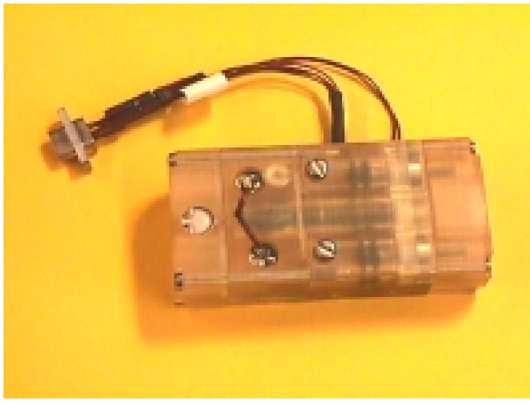

Figure 7
LIDIA-3 Experiment Unit for suspended cells

Recently, Fokker Space started the development of precursor elements for a modular space bioreactor, eventually aimed at use on the International Space Station. Under a contract from the European Space Agency (ESA), three experiments in the area of tissue engineering will be flown on the same sounding rocket as mentioned in the above. All three experiments are part of a wide Biomedical Application Research Contract signed between ESA and researchers from academia and industry (Ref. 9). The flight hardware for these experiments will be assembled in automated packages that are very much compatible with the accommodation capability of the desktop RPM. As an example, Figure 8 displays the concept for an assembly with nine modular reactors attached to an automated 'service system' on the dektop RPM.

The availability and application of simulated microgravity to tissue engineering research may prove to be very beneficial. Whereas the potential of rotating wall tissue engineering bioreactors is already well recognized in relation to 'true' microgravity (Refs. 10, 11), 'true' microgravity simulation as offered by the desktop RPM may well have an even more significant impact in this rapidly evolving biomedical application field.

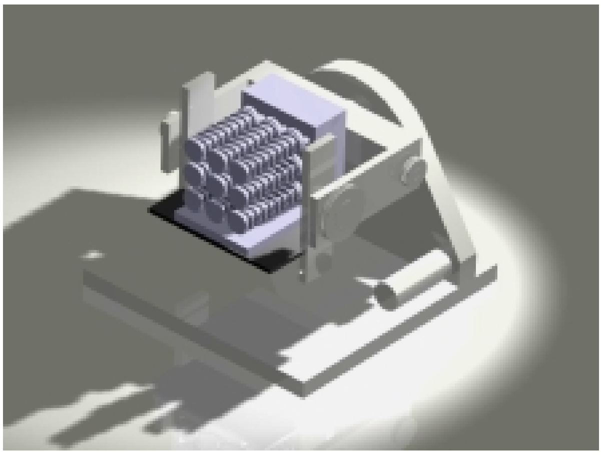

Figure 8
Concept of a bioreactor assembly on the desktop RPM

6. ACKNOWLEDGMENTS

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