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TWO HUNDRED PASSAGE THREE-WAY VALVE - FRACTION COLLECTOR

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ABSTRACT

This paper describes the design and operation of a fraction collector used to direct flow of separated biological materials from 197 capillary tubes to either a collection tray or to a waste tank. This mechanism uses a 28-volt dc gear motor driving twin cams to force 197 needles through a self-sealing silicone rubber septum, where they inject the material in 197 separate pockets in a collection tray. The position of the collector tray is sensed by two optical limit switches. The time sequences are controlled automatically by an electronics control monitoring module.

INTRODUCTION

This fraction collector is part of a biological materials processing unit that by 1987 is scheduled to lead to commercial marketing of new medicines unobtainable without the benefit of zero-g. The processing unit is called the Continuous Flow Electrophoresis System (CFES) and is currently being operated in the middeck of the Space Shuttle (Figure 1). While not new, the electrophoresis process has been greatly improved by a continuous flow arrangement yielding higher purity and greater quantities of certain proteins by separating them from other biological materials. Although many of the proteins are obtainable on earth, the processes used are so limited by gravity that only research quantities are available. In space, however, away from the adverse effects of gravity, it may be possible to obtain these proteins in the quantities and purities needed to effectively treat diseases.

Electrophoresis processing involves the separation of biological materials from their surrounding medium by passing a fluid between walls across which an electrical potential has been established (Figure 2). Different cells take on different charges and move to different positions across the column as the medium is pumped upward. These cells will stabilize in specific streams, where they will be collected by 197 collection tubes, each leading to a needle mounted in the fraction collector.

The Shuttle middeck processing unit consists of three modules: the Fluids System Module (FSM), which is the largest of the three, the Electronics Control and Monitoring Module (ECMM), and the Sample Storage Module (SSM). The fraction collector is located at the top of the FSM.

REQUIREMENTS

The function of the fraction collector is to divert all flow through 197 tubes from the separation column to either a waste tank or to a collector. The total flow rate is less than 100 ml/min at a system pressure that is less than 70.3 gms/cm² (one psig). Fluid viscosities greater than water but less than glue is to be expected. Dead volumes are minimized to prevent areas where biological growth could occur. Finally it should be inert to the biological products to prevent contamination.

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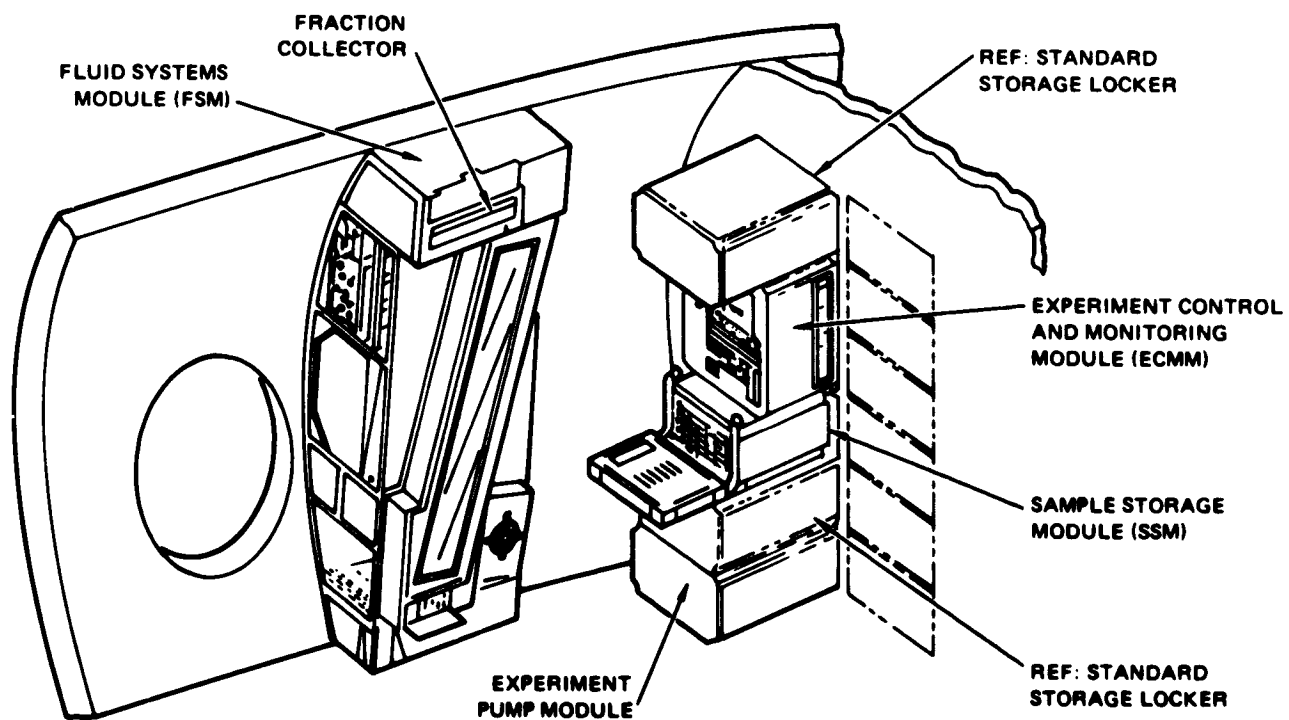
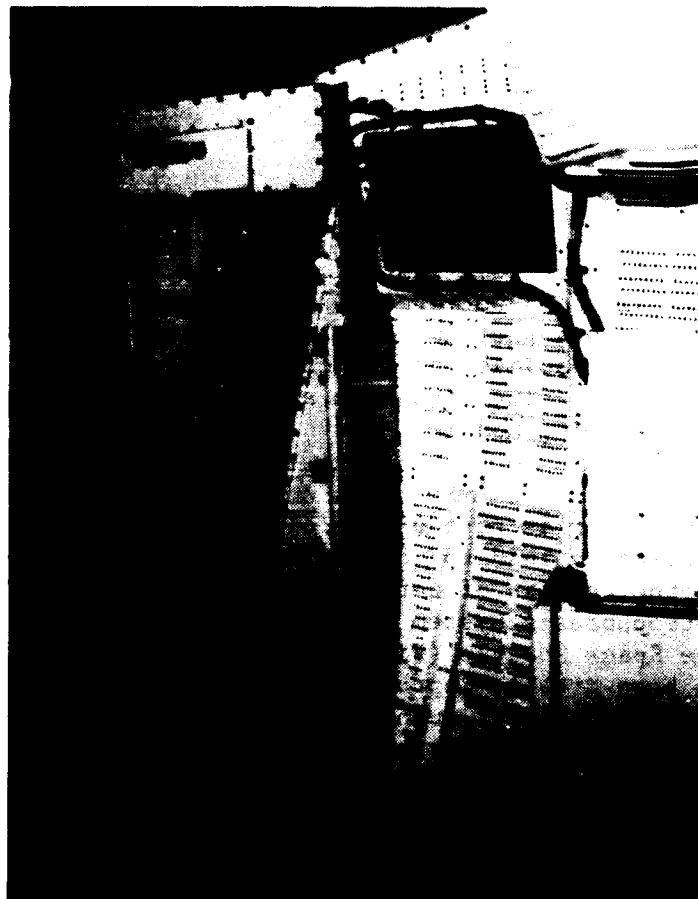
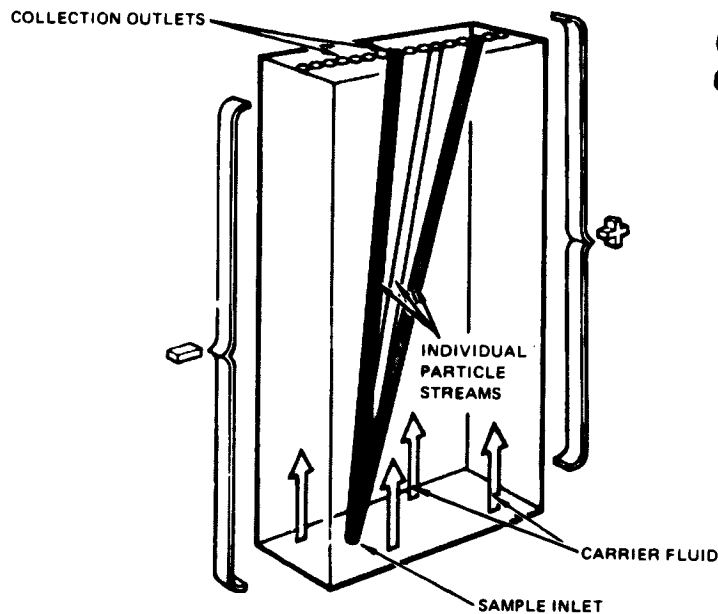


FIGURE 1 MIDDECK ELECTROPHORESIS SYSTEM



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CONTINUOUS FLOW ELECTROPHORESIS SEPARATES THE SAMPLE
INTO INDIVIDUAL PARTICLE STREAMS.

FIGURE 2 THE ELECTROPHORESIS SYSTEM

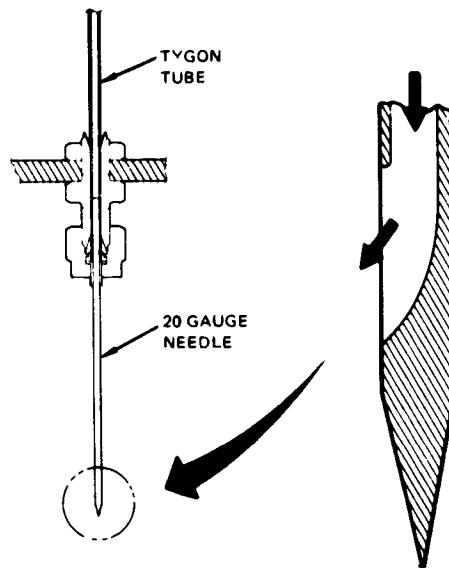
TRADE STUDIES

Each of the design concepts considered for the fraction collector involved the use of an array of 197 needles penetrating a self-sealing septum material. It is necessary for the septum material to reseal under system pressure after the needles are retracted. To verify this septum valving concept for use in the electrophoresis process middeck flight unit, development tests were performed to select the best needle configuration/septum material combination that requires the least penetration and retraction forces and has the best sealing qualities. In addition, a needle configuration that minimizes the possibility of septum coring was of primary importance to prevent septum leakage and to ensure all needles continue to flow even after septa penetration.

The selected needle configuration is a 20 gauge closed pencil point single side port arrangement (Figure 3). The side port is a slot that provides for a greater flow area than a round port without compromising the needle strength due to a reduced cross-section. The cone point aligns the forces through the needle centerline to ensure the needle will penetrate straight through the septa without straying. In addition, this side ported arrangement is self-cleaning with no dead volume.

The selected septum material is a 30 durometer medical grade silicone rubber. The maximum penetration force was measured at 771 grams (1.7 pounds) per needle on a single needle test at a rate of five cycles per minute. The retraction forces were not significantly different since most of the force is spent overcoming friction between the needle and the septa material.

It was discovered later in the development cycle that multiplying the penetration force from a single needle test times 197 needles is not a true representation of the total force required to penetrate the septum material with an array of 197 needles simultaneously. Instead, a factor of two should



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FIGURE 3 SELECTED NEEDLE CONFIGURATION

be applied to the calculated force using the method above. It is theorized that the additional force can be attributed mostly to the variations in needle straightness and needle parallelism causing interactive forces as they are forced through the septum material.

SYSTEM DESCRIPTION

Operation of the fraction collector (Figure 4) requires the astronaut to insert or remove collector cassettes. Other operations are handled automatically by the ECMM. The procedure is to open the access door to the collector area by turning two quarter turn latches, insert a cassette by engaging the two guide rails and pushing the cassette in until the ball plunger falls into place. A definite snapping action is felt at this point. The access door is then closed and latched. When the ECMM determines that collection is to take place the motor is energized forcing the septum material on top of the cassette against the septum material on the bottom of the waste manifold effecting a seal (Figure 5). Further upward travel forces the array of 197 needles through this stack of septum material into individual pockets in the cassette. When the mechanism reaches top dead center an optical limit switch is tripped to stop the motor. The mechanism will remain in this position for a predetermined amount of time, usually about 10-12 minutes as the cassette is being filled, then the motor is energized again forcing the waste manifold down causing the needles to withdraw from the cassette. The last part of the downward stroke is used to provide a gap between the cassette and the waste manifold to facilitate cassette removal and to seat the waste manifold against four stacks of four belleville washers. At bottom dead center another optical limit switch will stop the motor. At this time, the ECMM will prompt the astronaut to remove the cassette and place it back into the SSM.

The fraction collector consists of a welded aluminum structural frame supporting four guide shafts, the drive mechanism, the carriage assembly, a septum plug/spacer assembly, the waste manifold, the needle head, the 197 passage connect, two side latches, and finally a collector cassette that requires astronaut handling for insertion and removal.

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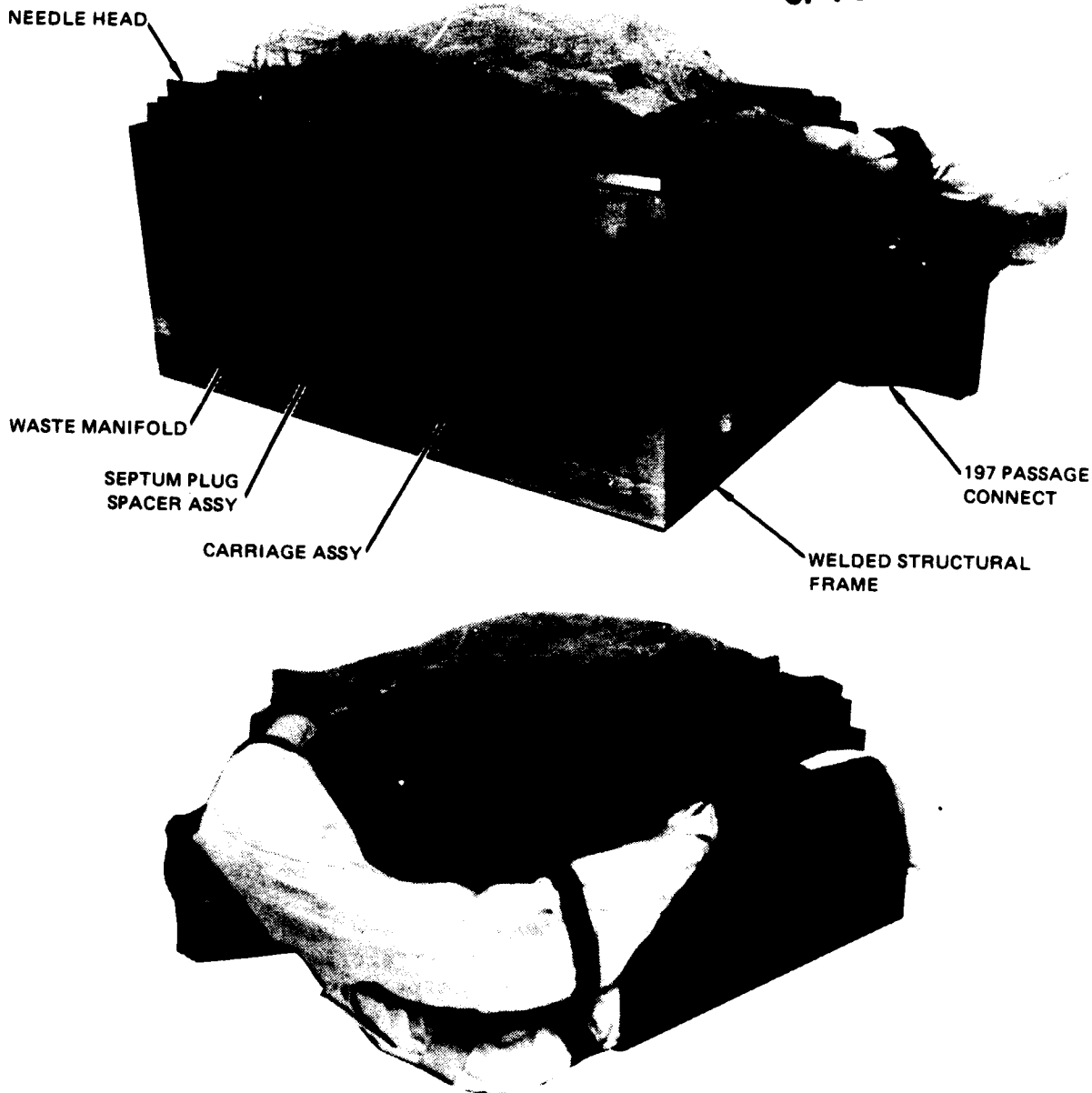


FIGURE 4 FRACTION COLLECTOR

The drive mechanism (Figure 6) includes a 28-volt dc gearmotor with a reduction ratio of 941/1. This motor is capable of delivering 2424 newtons (545 pounds) of vertical force at a rate of five cycles per minute at the maximum moment arm of one centimeter (.393 inch). At stall torque, 6494 newtons (1460 pounds) of vertical force is supplied by the motor at the maximum moment arm. The motor has a pinion gear mounted on the drive shaft that engages a line of three other pinions of equal diametric pitch to drive twin cams. With this gearing arrangement, the cams move in opposite rotational directions to keep the applied force symmetric about the four 1.27 centimeter (one half inch) diameter guide shafts. The cams are extra light duty aircraft bearings mounted off center to provide a total stroke of 1.99 centimeters (.785 inch).

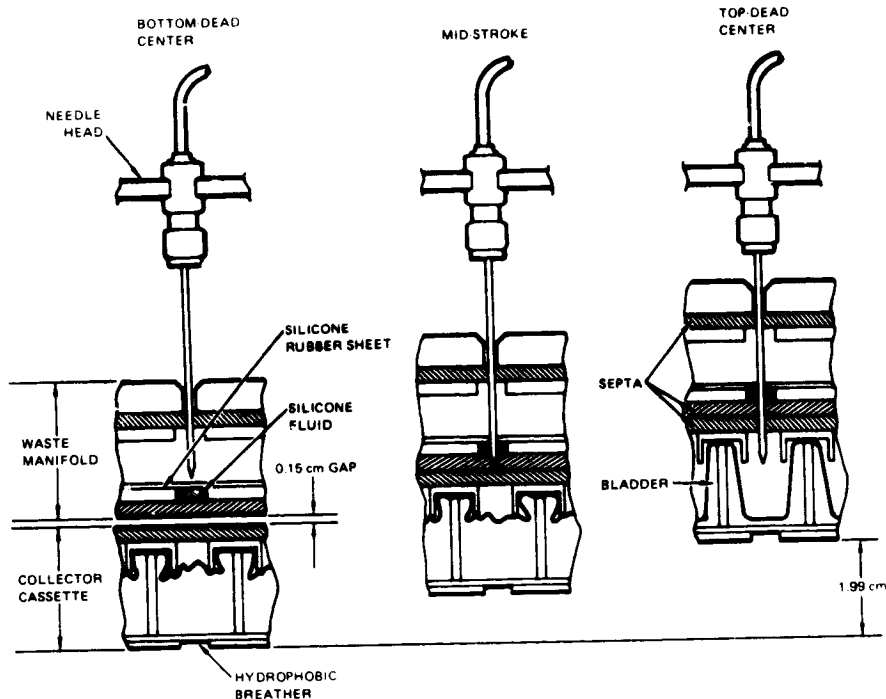


FIGURE 5 FRACTION COLLECTOR OPERATION

The vertical force is applied by the cams to the carriage assembly through two oblong shaped holes that allows the bearings to move freely from side-to-side as it rotates. This assembly provides a platform for insertion of collector cassettes up to 7.62 centimeters (three inches) in height. To date, only 2.54 centimeter (one inch) high cassettes have been used in flight; therefore, a spacer is required to make up the difference in height. Two bronze bearings are located on each of the four shafts and are spaced 6.10 centimeters (2.40 inches) apart to prevent binding. These bronze bearings are porous and are saturated with 350 centistokes silicone fluid for lubrication.

The septum plug/spacer assembly serves two purposes. First, it occupies the space necessary so that a 2.54 centimeter (one inch) high cassette can be accommodated. Second, it contains a mechanism consisting of two scissor jacks that raises a flat platform with 200 .953 centimeter (3/8 inch) square silicone rubber closed cell sponge pads that engage the needle penetrations in the septum material located on the bottom of the waste manifold. This is done by manually rotating two knobs located on the front of the spacer assembly. This was necessary as an insurance policy to prevent water seepage during launch and reentry. It was expected that 773 gms/cm² (11 psi) would be experienced during launch due to the water head, the launch g's, and the random vibration environment in the Shuttle middeck. The spacer contains a ball plunger to give a positive indication that the collector cassette is in position and properly aligned beneath the array of 197 needles.

The waste manifold is a shallow rectangular shaped stainless steel pan with a bolted on lid that collects the flow from all 197 tubes and directs

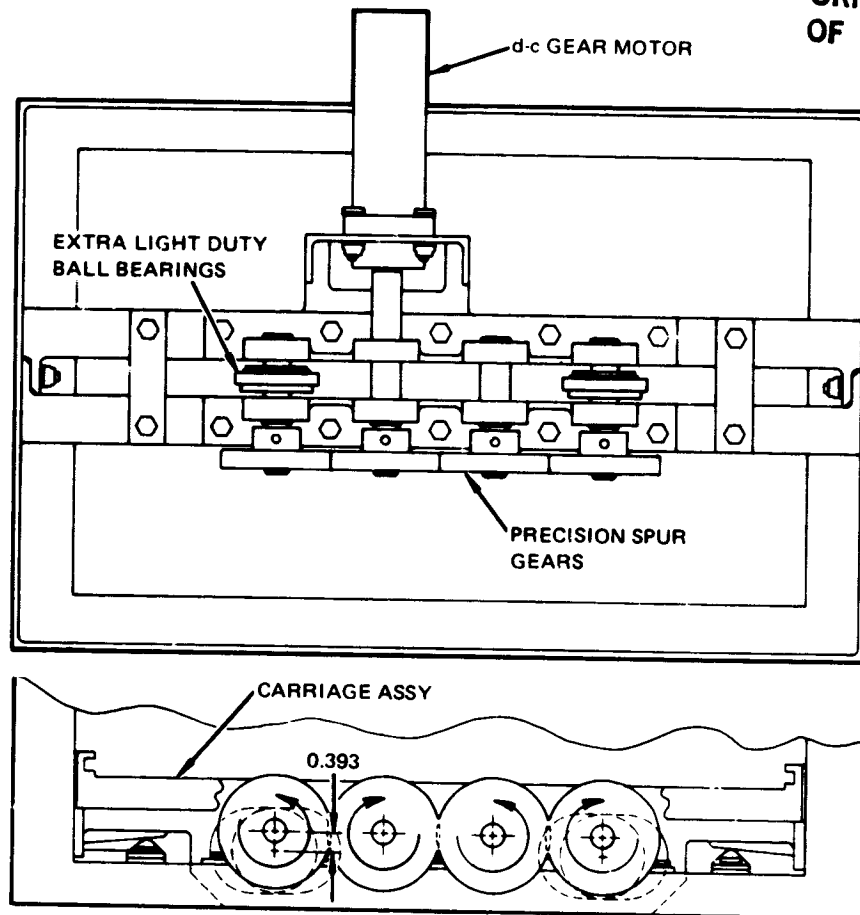


FIGURE 6 FRACTION COLLECTOR DRIVE MECHANISM

that flow to a waste tank when sample collections are not being made. Both the bottom and top of the waste manifold have an array of 200 .476 centimeters (3/16 inch) diameter holes covered over by a sheet of bonded on 30 durometer medical grade silicone rubber septum. One needle passes through the manifold in each of the 197 holes. Three holes are not used. The self sealing characteristics of the septum on the underside of the manifold was improved by injecting 1000 centistoke silicone fluid in the volume of each of the holes and capturing it with the septum on the underside and a .079 centimeter (1/32 inch) thick bonded on silicone rubber sheet on the inside. The top side septum which is sandwiched between two metal sheets provides a dynamic seal around each of the needles. The needles are never pulled out of this septum during operation. The top metal sheet provides a conical lead-in for each of the needles to facilitate needle installation.

The needles head (Figure 7) provides a mount for each needle assembly. An aligning tool was used when installing the needles into the needle head to ensure they were all parallel. The jam nuts were left loose enough to provide freedom of movement of the needle of about $\pm 10^\circ$ and then was locked in place with RTV 730 material. This was done to prevent any interaction between the needle due to nonparallelism or straightness variations that might cause a sideward force of the needle in the rubber resulting in leakage. This proved to be a necessary and a very important step in the assembly procedure.

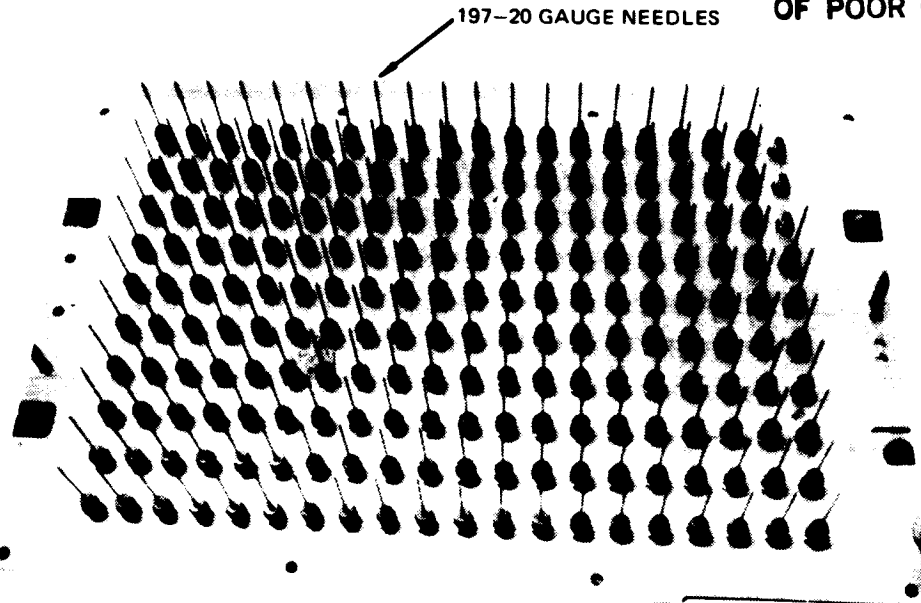


FIGURE 7 NEEDLE HEAD

A connect/disconnect is provided in the 197 tubes between the separation column and the fraction collector to facilitate removal/installation of either unit. The connect is 8.26 centimeters (3.25 inches) in diameter and consists of two mating stainless steel halves that are keyed together with dowel pins to ensure proper continuity of each tube. A thin .079 centimeter (1/32 inch) gasket is placed between the halves. The gasket seals both to the outside and around each of the 197 holes. This assembly is held together with a marman V-band clamp. Each tube was placed through the connect to the interface plane and then all were bonded in place with Hartel two part epoxy. This arrangement reduced the dead volume to near zero and also minimized metal contact with the buffer solution.

The two side latches (Figure 8) provide two functions. First, they pull the waste manifold off of the needles on the down-stroke. Second, they lock the manifold down when the cams reach bottom dead center. This prevents the manifold from getting excited during the vibration environment of launch and reentry.

Each latch consists of a ratchet, which is bolted to the waste manifold, a pawl, that is free to rotate about a clamp-up bushing on the carriage assembly and a fulcrum, that forces the pawl to rotate on the down-stroke.

The ratchet has two surfaces. On the up-stroke the pawl elevates and rotates up to the top surface of the ratchet. On the down-stroke the pawl pulls against the ratchet forcing the waste manifold off of the needles. During the last part of the downward motion the pawl is forced to rotate off of the top surface of the ratchet to the bottom surface, by the fulcrum, providing a gap between the waste manifold and the collector cassette facilitating removal and insertion of the cassette. The cams continue to rotate until bottom dead center is reached at which time the pawls pull the waste manifold against four stacks of four Belleville washers. This provides the clamp-up force required to hold the waste manifold during launch and reentry dynamic environments.

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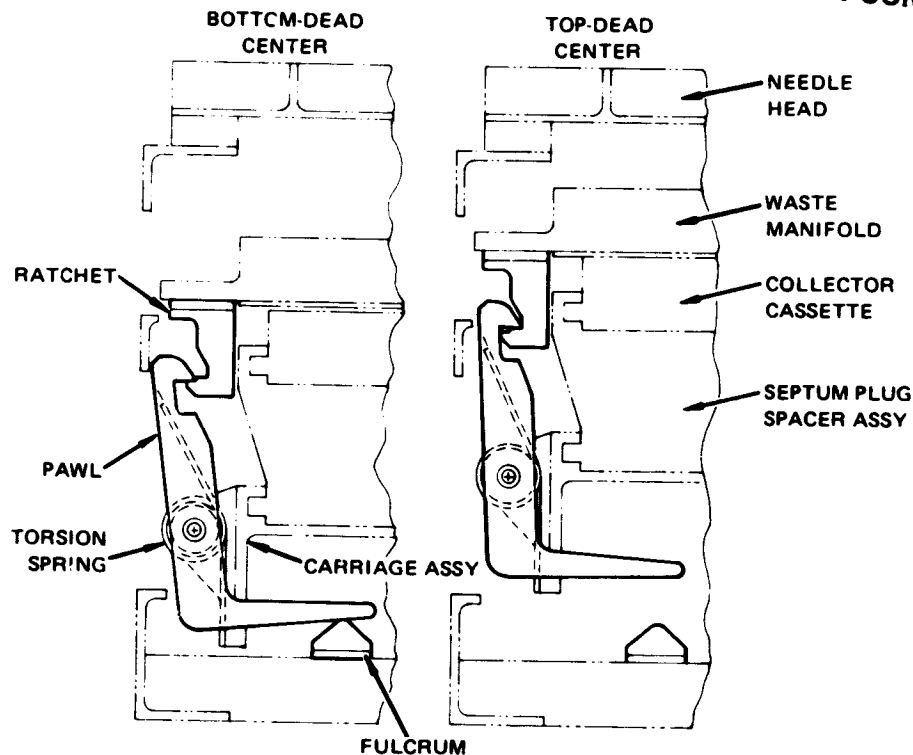


FIGURE 8 SIDE LATCH ARRANGEMENT

The collector cassette (Figure 9) resembles an egg carton consisting of a molded medical grade polyvinyl chloride bladder with 200 individual pockets in a 10 by 20 array covered with a polycarbonate sheet that is bonded to the ridges around the opening of each of the pockets. The assembly is then covered with a sheet of septum material that is bonded in place sealing around each pocket. These pockets are evacuated prior to use. Each pocket holds about 2.5ml of fluid. A machined aluminum frame provides the grid work for each of the pockets. The frame also has rails on all four sides that either engage the carriage assembly or the SSM where the cassettes are stored when not in use. The bottom of the cassette frame is covered by a sheet of hydrophobic material which is held in place by a bolted on aluminum sheet with 200 holes. As the pockets are being filled this hydrophobic material will vent the displaced air but prevent any water from passing through.

SAFETY ASPECTS

Several steps were taken to ensure the safety of the astronaut while interfacing with the collector. The fraction collector is rendered inoperable when either the access door is opened or when there is no cassette in place. This is accomplished by a plunger switch sensing the door position and a micro-switch with a roller leaf that engages a cammed surface on the cassette guide rail. In addition, the needle points are not exposed to the astronaut when he is inserting or removing a cassette, but are inside the waste manifold during this operation.

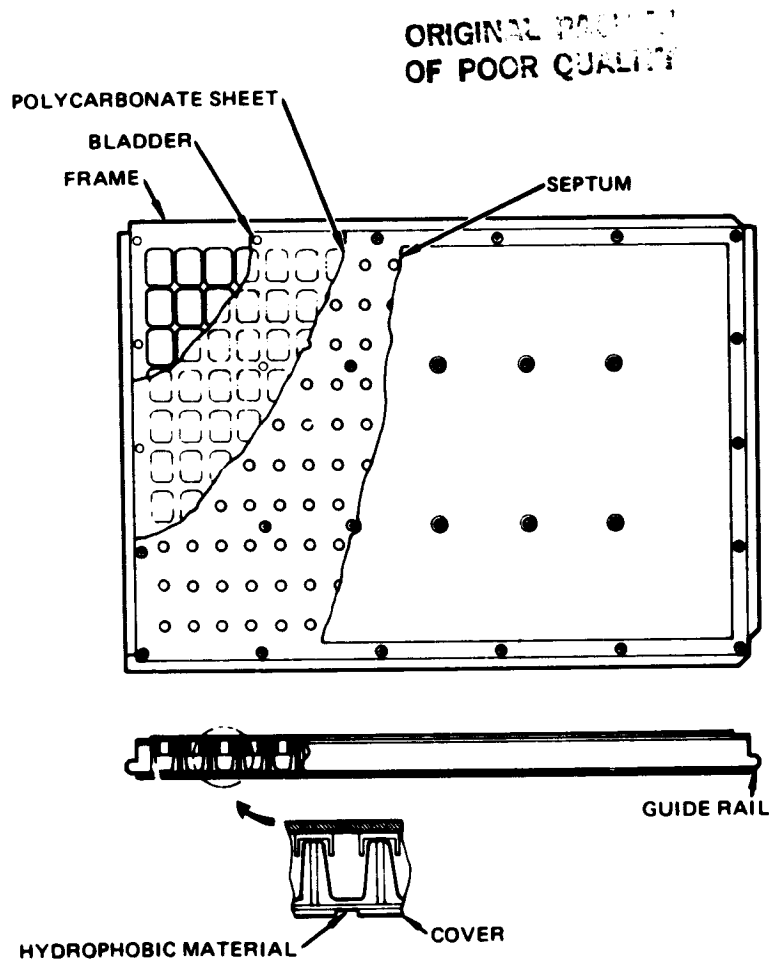


FIGURE 9 COLLECTOR CASSETTE

CONCLUSIONS

A two hundred passage three-way valve has been developed that collects the biological fractions from the continuous flow electrophoresis system. The forces required to drive an array of 197 20-gauge needles through a stack of septum material (.313 inch thick) is approximately two times the single needle force times 197.