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Remenyik

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[54] **CENTRIFUGE FOR THE INTERACTING OF CONTINUOUS FLOWS**

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[51] **Int. Cl.** **B04b 15/02**

[58] **Field of Search** 233/15, 31, 37, 43, 46, 233/32, 44, 27, 28, 33

[56] **References Cited**

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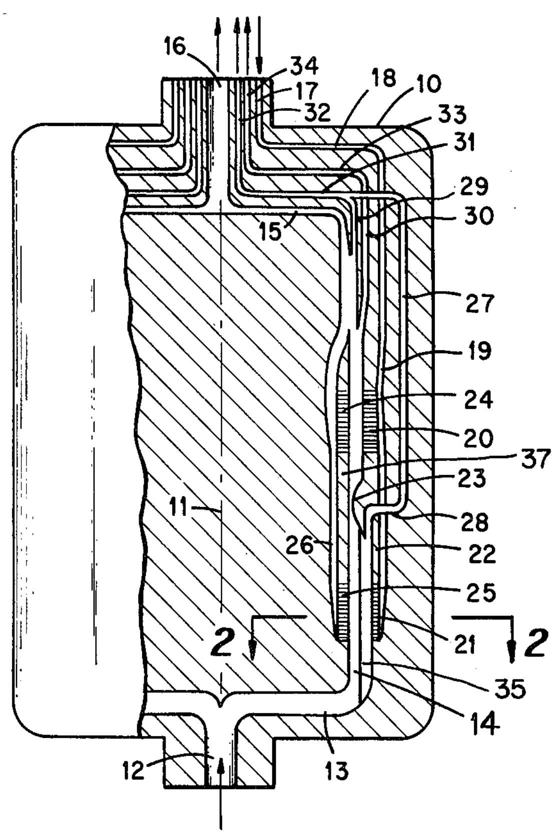
[57] **ABSTRACT**

A liquid centrifuge rotor for inducing the interaction of a plurality of substances flowing continuously therethrough, separating products that result from this interaction and continuously removing these products. Plural flow passages, arranged as concentric cylinders near the periphery of the rotor, are interconnected with either porous walls or open portions in the walls for controlling velocities of radial flow between flow passages. The design thus permits countercurrent axial flow as well as radial cross-flow. Applications of this rotor are described for the continuous separation of particulate blood components via centrifugation combined with plasma cross-flow, and the oxygenation of blood as in a heart-lung machine.

5 Claims, 2 Drawing Figures



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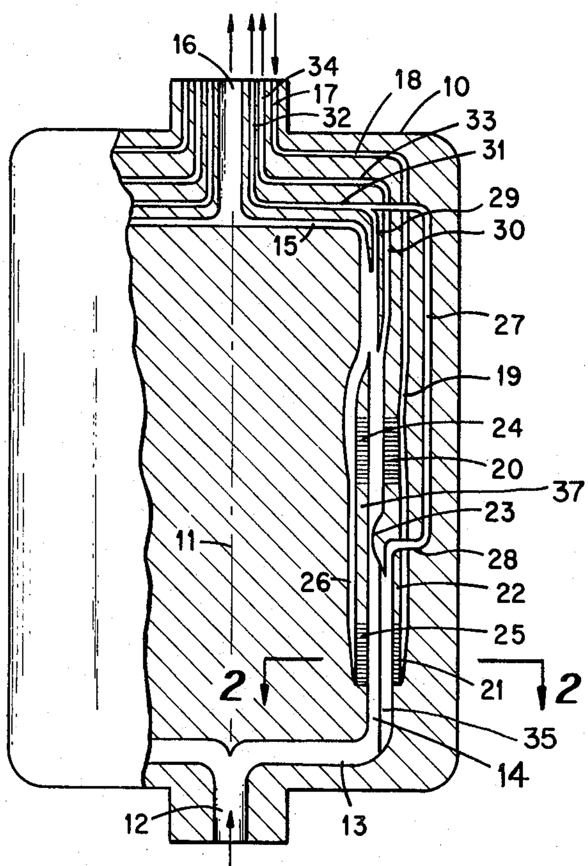

Fig. 1

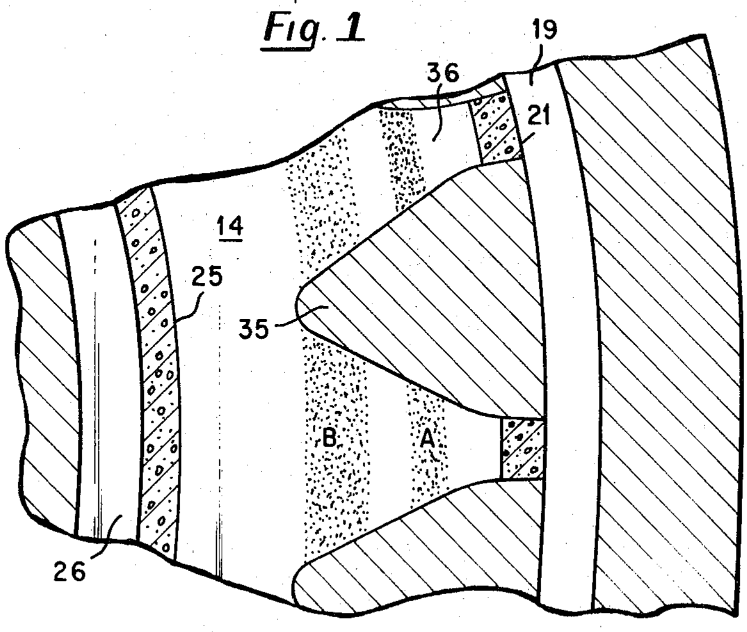

Fig. 2

CENTRIFUGE FOR THE INTERACTING OF CONTINUOUS FLOWS

BACKGROUND OF THE INVENTION

The art of continuous-flow liquid centrifuges has been advanced substantially in recent years whereby rather intricate analytical-type methods may be easily accomplished. Typical of the centrifuges for these purposes are described in U.S. Pat. Nos. 3,536,253, 3,547,547 and 3,556,967. Additional information is described in the National Cancer Institute Monograph 21, "The Development of Zonal Centrifuges and Ancilliary Systems for Tissue Fractionation and Analysis," U.S. Dept. of Health, Education and Welfare, Public Health Service. Other pertinent references are: "The Ultracentrifuge," T. Svedberg and K. O. Pedersen, Oxford University Press, Oxford, England (1940); and "Counter-Streaming Centrifuge for the Separation of Cells or Cell Fragments of Different Sizes," P. E. Lindahl and E. Nyberg, IVA; Tidskrift For Teknisk-Vetenskaplig Forskning, 26, p. 309 (1955).

Centrifuges for separating the particulate components of blood are described in reports submitted by Abcor, Inc., Cambridge, Mass., to the National Cancer Institute, N.I.H., under Contract NIH-20-2239. The fundamental centrifuge for these studies is Model CL manufactured by International Equipment Corporation. A similar centrifuge was utilized in a research contract between International Business Machine Corp. and the National Cancer Institute.

Continuous flow centrifuge rotors of the prior art generally fall into one of three classes. In all of these types, entrance and exit is made at or near the axis of rotation, frequently at both ends. In one class of rotor, the separation chamber is essentially parallel to the axis of rotation, often a cylindrical chamber located at some distance from the axis. During passage of fluid through this chamber, dense suspensions tend to concentrate at or near the outer wall of the chamber and less dense ones, closer to the axis of rotation. One or more of these fractions may be individually removed by several conventional techniques after separations have been completed.

In the second class of rotors, the reaction vessel or chamber is essentially oriented in a radial position within the rotor. Usually the more dense fractions are left at the position farthest from the axis, and the less dense fractions leave with the carrier liquid at or near the axis. The more dense fractions may later be removed by a separate flow of fluid through the rotor.

A third, or intermediate, class of rotors has separation chambers in the rotors such that the principal flow directions are inclined at angles, to the axis, between 0° and 90°.

In most continuous flow centrifuges, only the fluid carrying the unseparated mixture of suspensions is flowing continuously through the rotor. The various separated suspensions band in zones and remain there until the flow of the mixture is turned off. The position of the zones is determined by the densities and fluid mechanical properties of the suspended particles. These separated components of the mixture are removed from the rotor after the flow of the mixture has been interrupted.

Present centrifuges from which separated blood components (red blood cells, white blood cells and plasma) are removed continuously have unsatisfactory efficiencies, usually less than about 20%. Furthermore, may types of desired interactions are not possible in these prior art devices.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a vertical sectional drawing, in schematic form, of a centrifuge rotor to accomplish the interacting of at least two continuous flows of fluids; and

FIG. 2 is an enlarged sectional drawing of a portion of the rotor of FIG. 1 taken at 2—2 thereof.

SUMMARY OF THE INVENTION

My improved centrifuge rotor is an elongate cylinder having a plurality of slender concentric vessels arranged near the periphery thereof. Plural inlet and outlet ports are provided at one or both ends of the rotor, near to and concentric with the axis of rotation, whereby two or more fluids may be passed continuously through adjacent vessels. Small openings between the concentric vessels permit radial flow, inward or outward, to control the radial velocity of fluids to induce the interaction between the plural fluids and the removal of certain products of the interaction. Separation of the products is achieved by the combined centrifugal field acting upon components of differing densities and by drag forces produced by the cross-flow.

DETAILED DESCRIPTION

Referring now to FIG. 1, a rotor body **10** is caused to be rotated about axis of revolution **11** by any suitable means including conventional bearings, seals and drive motor (not shown). A first fluid inlet **12** is positioned on the axis at either end of body **10** (shown here at the bottom) and communicates with radially-extending passageway **13** leading to a primary slender cylindrical reaction vessel **14**. By slender I mean having a radial dimension that is small with respect to the axial dimension. The upper end of reaction vessel **14** connects to radial passageway **15** which, in turn, connects with outlet **16** on the axis **11** at the top of body **10**. A second fluid inlet **17** is concentric with outlet **16** and communicates with passageway **18** leading to slender cylindrical chamber **19**. The vessel **14** and chamber **19** are separated by a wall **22**. Small interconnections **20, 21** in wall **22** between chamber **19** and reaction vessel **14** join chamber **19** to reaction vessel **14** on either side of a constriction formed by ridge **23** projecting into vessel **14**. The ridge **23** may extend into reaction vessel **14** from either the inner or outer wall thereof. Similar small interconnections **24, 25** through a wall **37** join reaction vessel **14** to an inwardly disposed slender cylindrical chamber **26** for purposes discussed below.

An outer slender concentric channel **27** is connected to reaction vessel **14**, by passageway **28**, on the upstream side of the ridge **23**, and additional channels **29, 30** connect to vessel **14** for purposes described hereinafter. Channel **27** and channel **29** connect to a common passageway **31** leading to an outlet **32** concentric with outlet **16**. Channel **30** connects with passageway **33** which, in turn, connects with concentric outlet **34**.

The rotor of my design may be fabricated from any material which is compatible with the fluids to be utilized in the separations. Since the rotor is not intended for high-speed operation, even certain inert plastics may be utilized to simplify fabrication procedures. Alternatively, the bulk of the rotor may be fabricated of either metal or plastic, with all cavity surfaces coated with unreactive materials. Typically, the rotor may be fabricated in several portions to produce the required cavities and thereafter the portions joined to create the entire rotor. In order to minimize the number of rotary seals, all inlets and outlets for the rotor preferably may be at one end of the rotor. The openings or pores **20, 21 24** and **25** are in the form of inserts of sheets of porous materials or like materials. The pore size is greater than the size of red blood cells which is about 7–8μ. Thus the pore size is about 10μ or greater.

The space between walls in vessel **14** and chambers **19, 26** may vary typically between 1 mm and 5 mm. To meet external constraints, rotor lengths may be 15 to 50 cm and diameters 10 to 20 cm. A typical rotor speed is 1000 rpm. It will be recognized that exact parameters of size and speed are determined by particular applications of my rotor design.

The concentric relationship of the various chambers with the reaction vessel **14** is illustrated also in FIG. **2** which is an enlarged portion of a transverse section taken through the rotor at **2—2** of FIG. **1** perpendicular to the axis of rotation of rotor **10**. The details of the passages are more clearly illustrated in this enlargement. The wall **22** between channel **19** and reaction vessel **14** is made up of a plurality of generally teardrop shaped sections **35** to thereby form radially-oriented channels **36** running in an axial direction. The portion of channels **36** most distant from the axis of rotor **10** are narrow, and interconnections or pores **21** communicate to these channels at that point. The shape of channel **36** is chosen to produce the proper radial (inward) velocity gradient to fluids entering the periphery of the channel whereby drag forces are produced on particles attempting to move radially outwardly. The pores **21** act as diffusers to give the high initial velocity. Reduced velocity and thus drag forces exist inward from that radius due to the widening of channel **36**, as shown. The effect of this construction will become more apparent from the hereinafter-described separation of particulate blood components.

In the figures, reaction vessel **14** and concentric chambers **19, 26,** and channel **27** are illustrated as being completely annular in rotor **10.** While this may be preferred for high volume flow through the rotor, these elements may also be subdivided by axially-extending septa if desired for fabrication requirements. Likewise, the radially-extending passageways, e.g., **13,** may be subdivided.

The rotor of my design may be utilized for inducing many interaction reactions such as those between whole blood and blood components. Typical is the separation of particulate blood components from whole blood by centrifugation with plasma cross-flow. For this separation, and referring to FIGS. **1** and **2,** whole blood is introduced into reaction vessel **14** through inlet **12** and passageway **13,** while plasma is fed through inlet **17** and passageway **18** into chamber **19.** Plasma flows through the openings (small pores) **21** to mix with the whole blood in vessel **14.** Due to the centrifugal effects and the counter-acting radial component of the plasma stream, large rouleaux (aggregate) of red blood cells separate from the whole blood stream and collect along the outer wall of reaction vessel **14** (in channels **36**) in a band designated as A in FIG. **2.** These then move axially and are withdrawn through passageway **28** into channel **27** where they later leave the rotor **10** through outlet **32.** Concurrently, plasma, platelets, single red blood cells and small rouleaux of red blood cells pass through pores **25** into chamber **26.**

The remaining portion of the blood stream in reaction vessel **14,** as in band B of FIG. **2** which is primarily white blood cells and intermediate rouleaux of red blood cells, passes ridge **23** where remaining rouleaux are broken by shear forces. Additional plasma enters the stream through pores **20** and additional separation occurs as a function of centrifugation and drag forces. The white cells are the fastest sedimenting component in this region and are thus drawn off into channel **30** so as to leave rotor **10** thorugh outlet **34.** Since the red cells are more dense than plasma, they sediment and are removed through channel **29** and flow, with the large rouleaux and some plasma, through passageway **31** and outlet **32.** Remaining plasma then leaves through outlet **16.**

The separation and collection of white blood cells, as described above, is highly useful in the treatment of persons afflicted with leukemia. These persons often require the addition of the order of 10^{10} white blood cells per day. This quantity of cells necessitates the processing, with presently available efficiencies of the prior art, of the order of 10 liters of blood or the equivalent of about 20 donors if batches of collected blood are to be processed. However, a healthy donor can spare that quantity of white blood cells if there is no substantial loss of red blood cells. Accordingly, my rotor can be utilized to continuously separate the particulate components of a donor's blood and return the plasma and red blood cells to the donor without contact with any deleterious substance such as gases or chemicals.

For this separation, a whole blood flow rate into the rotor is about 100 ml/min. and the recirculating plasma feed rate is about 200 ml/min. These fluids are subjected to a centrifugal acceleration force of about 50G to bring about the intereaction and the subsequent separation of the components as described above.

A further application of my rotor design, in a simplified form, is that of performing the functions of a heart-lung machine. For this application, the ridge **23** is not required nor are the majority of various channels to receive separated components. The whole blood is pumped into reaction vessel **14,** as above. An oxygen-rich liquid of lower density than the whole blood, such as oxygenated plasma, is admitted into chamber **19** where it then passes inwardly through pores **20, 21** to perfuse the blood, thereby exchanging oxygen to the red blood cells. Oxygen-depleted liquid leaves the blood stream through pores **24, 25** into chamber **26.** Oxygenated blood then leaves the rotor through channel **29** (and outlet **32**) and the oxygen depleted liquid is removed through outlet **16.** In this manner the centrifugal field accelerates the exchange of oxygen by accelerating the transition of the oxygen-rich liquid (plasma) through the whole blood. This then reduces the amount of blood that is outside a patient at any one time.

In any treatment of blood, particularly where all or portions thereof are to be reinjected into patients, care must be exercised to minimize (preferably prevent) contact with an adverse environment such as gases, e.g., air. Otherwise there is a detrimental reaction between the blood and the gases, resulting in cell deterioration, as well as the entrapment of gas bubbles in the blood, causing embolism. In my rotor design, blood is not exposed to air or other gas interface at any time. Prevention of contact is accomplished by first filling (and flushing) the rotor passages with a fluid which is compatible with blood constituents. This fluid may be, for example, additional blood plasma. A flow of whole blood then displaces the plasma and the above-described procedures are carried out. Thus, the desirable products from my rotor may be used directly for patients permitting a closed flow-path from the patient back to the patient or from a donor back to a patient and to the donor as desired. Appropriate pumps would be combined with my centrifuge to bring about the desired flow.

Although my rotor has been described for applications wherein there is interaction between whole blood and plasma or other second liquid, it is generally applicable to the interaction of other liquids where centrifugal and drag forces can be combined to sediment products of the interaction and provide for the continuous removal of the products.

I claim:

1. A centrifuge rotor for effecting interaction between continuously flowing first and second liquid streams and for continuously removing the products of the interaction, which comprises: a cylindrical rotor body symmetrical about an axis of rotation; a slender annular reaction vessel within the rotor body coaxial with the axis of rotation; a first liquid inlet to the rotor body; an axially-symmetrical first inlet passage peripherally connecting the first inlet with one end of the reaction vessel for uniformly and continuously admitting the first liquid; a slender annular first chamber within the body coaxial with the reaction vessel and spaced farther from the axis of rotation; a second liquid inlet to the rotor body; a second inlet passage peripherally connecting the second inlet with the first chamber for uniformly and continuously admitting the second liquid; a plurality of radially-oriented first openings interconnecting the first chamber and the reaction vessel whereby the second liquid is continuously in cross-flow relationship with the first liquid to bring about interaction therebetween; an axially-symmetrical first outlet passage connected to the second end of the reaction vessel to continuously remove one interaction product; an axially-symmetrical second outlet passage connected to the periphery of the reaction vessel at a greater distance from the axis of rotation to remove another interaction product; and outlets from the rotor body connected to the first and second outlet passages.

2. The rotor of claim **1** further comprising a plurality of axially-extending channels in the reaction vessel along a wall farthest removed from the axis of rotation, the peripheral width of these channels decreasing at increased distances from the axis of rotation; and wherein the first openings from the first chamber communicate with the most convergent portion of the channels.

3. The rotor of claim **2** further comprising: an annular ridge extending radially from one wall of the reaction vessel in a plane perpendicular to the axis of rotation; and an axially-symmetrical third outlet passage peripherally connected to the reaction vessel at a position between the annular ridge and the first inlet passage, the third outlet being at a greater distance from the axis of rotation than the second outlet.

4. The rotor of claim **2** further comprising a slender annular second chamber coaxial with the reaction vessel and spaced toward the axis of rotation from the reaction vessel, and a plurality of radially-oriented second openings interconnecting the reaction vessel and the second chamber.

5. The rotor of claim **4** wherein the radial dimension of the reaction vessel and the first and second chambers is about 1 to 5 mm, wherein the rotor axial length is about 15 to 50 cm and wherein the size of the first and second openings is at least 10 μ.

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