April 30, 1968 M. J. FULWYLER 3,380,584

PARTICLE SEPARATOR

Filed June 4, 1965 5 Sheets-Sheet 1

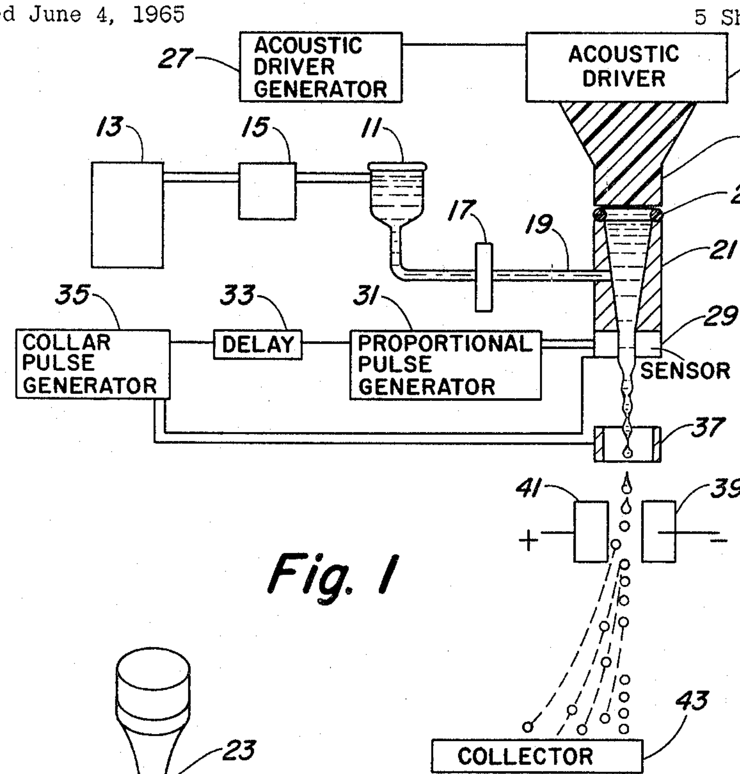

Fig. 1

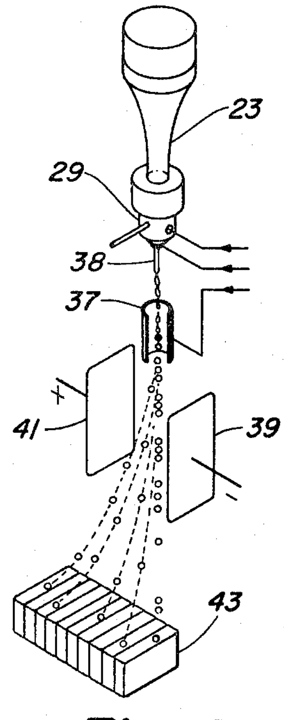

Fig. 2

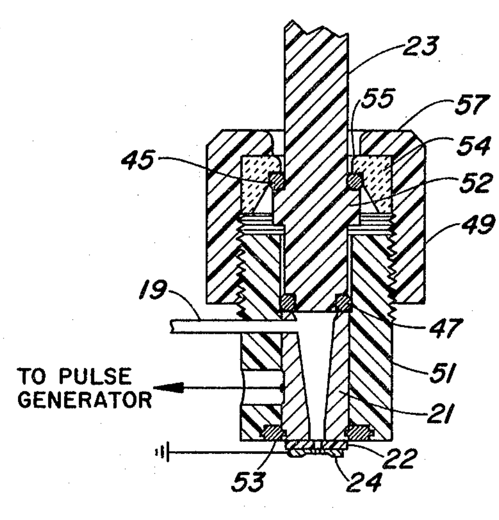

Fig. 3

INVENTOR.
Mack J. Fulwyler

BY

Roland A. Anderson
Attorney

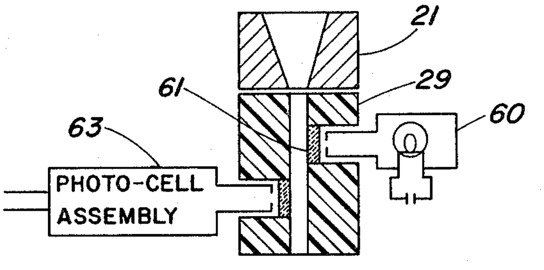

Fig. 4

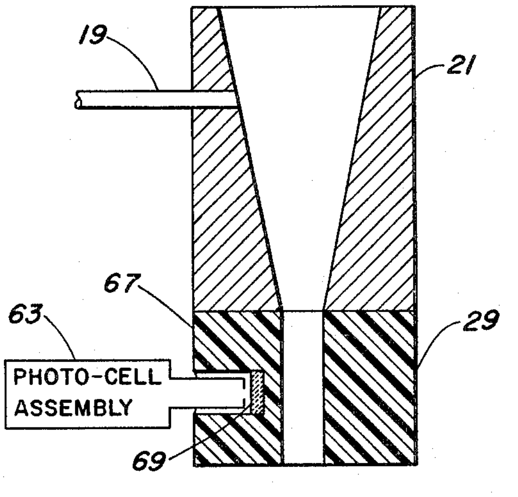

Fig. 5

INVENTOR.
Mack J. Fulwyler
BY
Roland A. Anderson
Attorney

PARTICLE SEPARATOR

Filed June 4, 1965 5 Sheets-Sheet 3

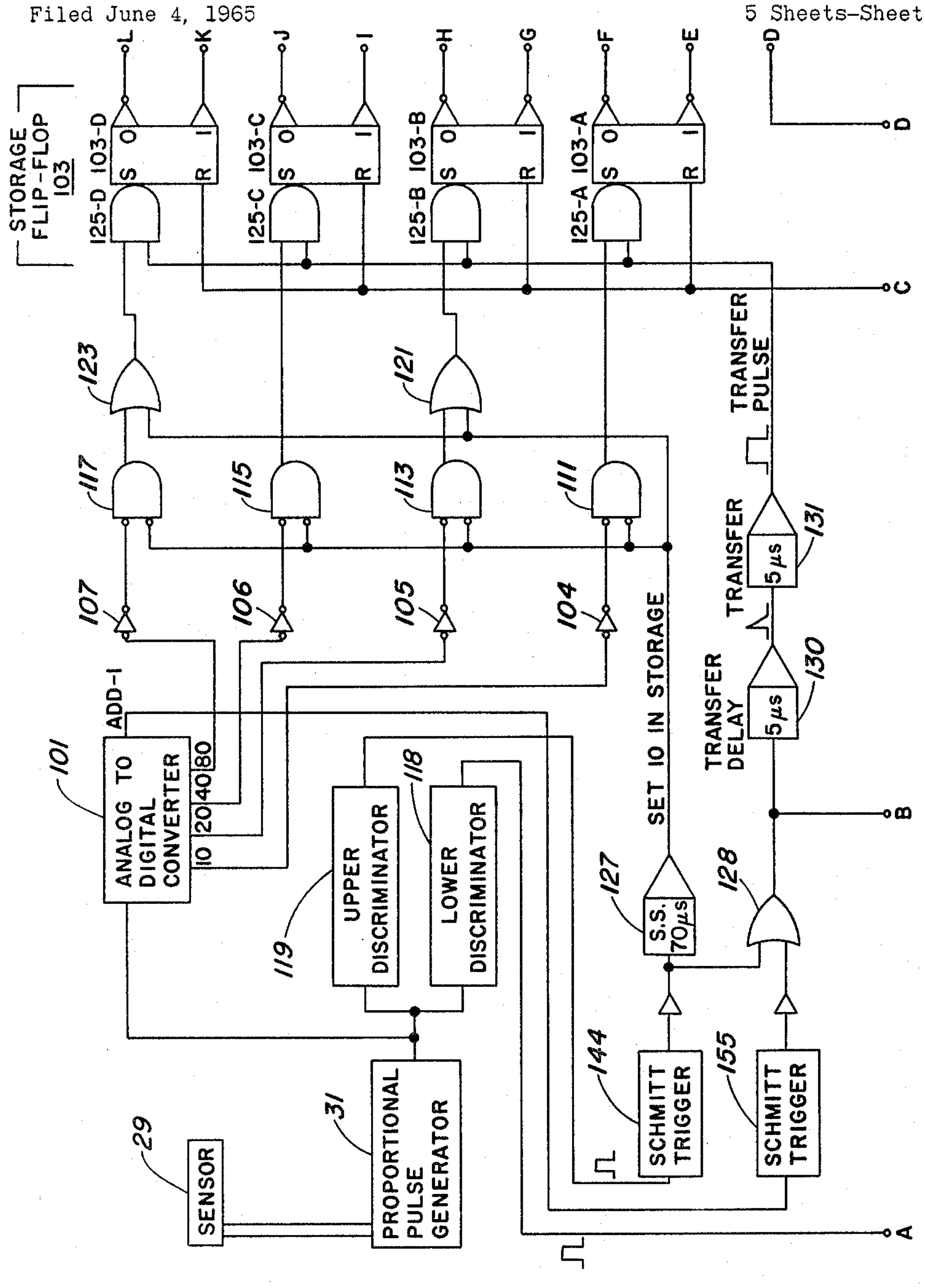

Fig. 6

INVENTOR.
Mack J. Fulwyler

BY
Roland A. Anderson
Attorney

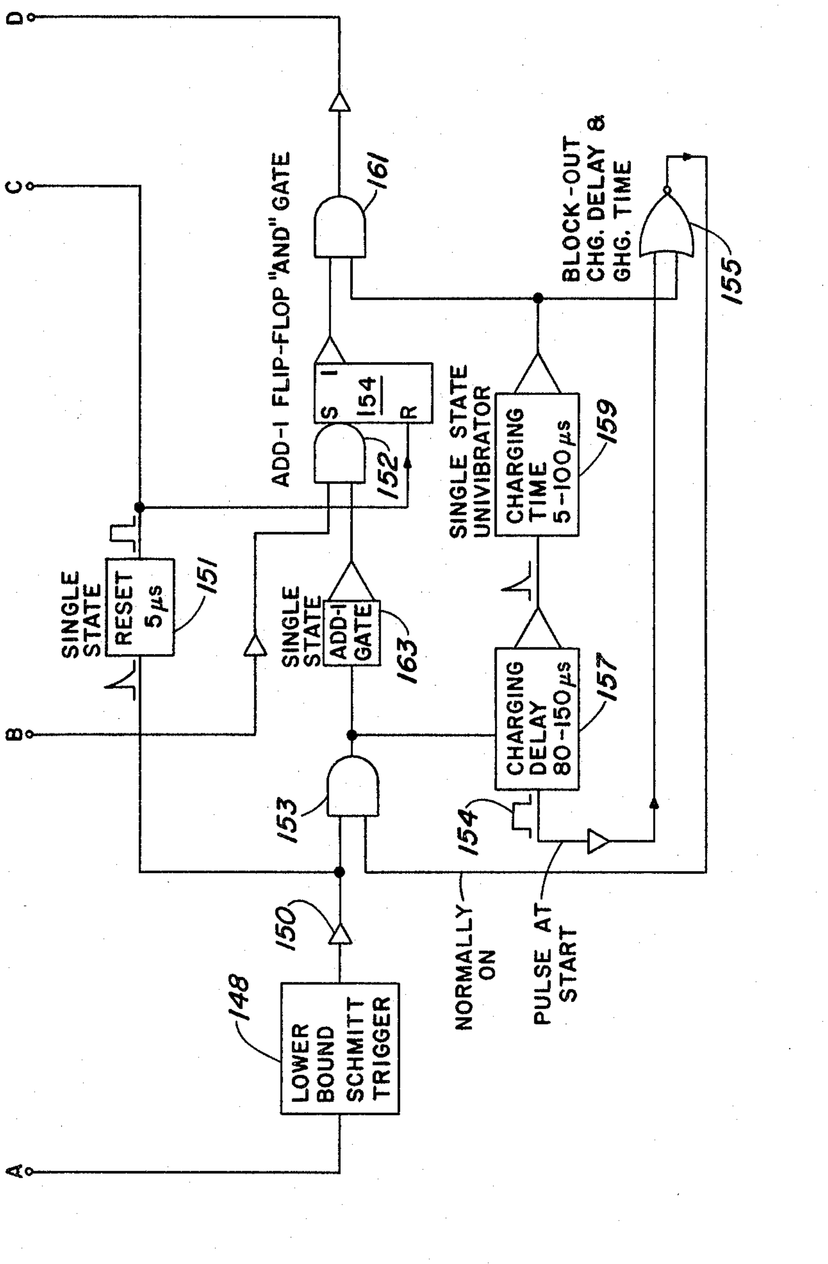

Fig. 7

INVENTOR.
Mack J. Fulwyler

BY

Robert A. Anderson
Attorney

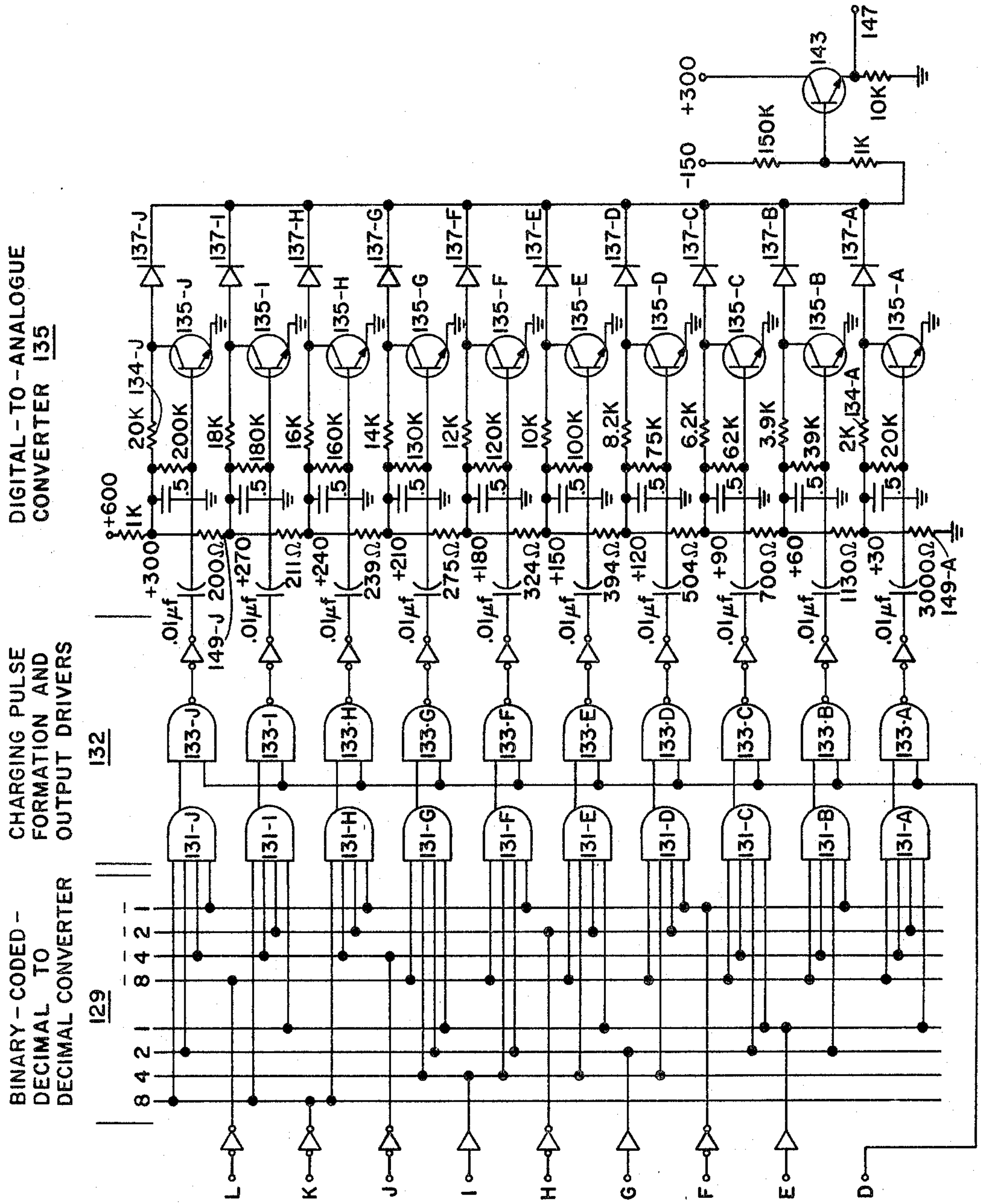

Fig. 8

INVENTOR.
Mack J. Fulwyler
BY
Roland A. Anderson
Attorney

3,380,584

PARTICLE SEPARATOR

Mack J. Fulwyler, Los Alamos, N. Mex., assignor to the United States of America as represented by the United States Atomic Energy Commission

Filed June 4, 1965, Ser. No. 461,566
3 Claims. (Cl. 209—3)

This invention relates to an apparatus and method for sorting minute particles present in a suspension fluid in accordance with a selected characteristic. The selected characteristic may be size, presence of radioactivity, color, fluorescence, light transparency or opaqueness or in fact any characteristic which can be translated into an analogue electrical quantity.

An apparatus capable of sorting minute particles in accordance with distinctive characteristics among the particles themselves has many important uses. For example, in the field of biology, it would be useful to sort blood cells in accordance with size. In investigations of carcinoma, it is useful to separate cancer cells from normal cells as indicated by size, radioactivity or luminescence from normal cells. In the separation of rare metals from ores, it would be useful to comminute the material and separate reflective metal particles from the refuse on the basis of reflectivity translated by electro-optic means into analogue electrical quantities.

In the present state of the art, means are available for counting minute particles in a fluid but no apparatus or method is available for physically sorting and counting such particles in accordance with the magnitude of a selected characteristic.

It is accordingly a principal object of the present invention to provide a method and apparatus for detecting minute particles in a suspension fluid and to physically separate such particles into groupings of particles having a common characteristic.

It is a further object of my invention to provide improved apparatus for separating a moving stream of fluid containing suspended particles into separate droplets and to deflect such droplets into separate receptacles each designated to catch and retain droplets containing particles of a predetermined characteristic.

The above and additional objects and advantages of the present invention will be made evident as the specification proceeds with reference to the following specification and claims and the illustrations in the accompanying drawings.

Referring to the drawings:

FIGURE 1 is a schematic diagram of a simplified system of the present invention;

FIGURE 2 is a pictorial illustration of a nozzle assembly and deflection system;

FIGURE 3 is a detailed cross-sectional view of a preferred nozzle adapted to develop the jet and in response to each particle passing through the nozzle to generate an analogue electrical quantity;

FIGURE 4 is a cross-sectional view of the nozzle adapted to generate analogue electrical quantities in response to luminescence of particles;

FIGURE 5 is a cross-sectional view of the nozzle adapted to generate electrical analogue quantities in response to radioactivity of particles; and

FIGURES 6, 7 and 8 are an electrical schematic diagram of a control system for a working embodiment of the invention.

The present invention in its broad sense is a combination of means for converting a particle characteristic into an electrical analogue quantity, and means for deflecting the particle in accordance with the electrical quantity into a corresponding repository. For example, the separation of biological cells can be accomplished by combining, in accordance with the teachings of this invention, the teachings of W. H. Coulter in Patent 2,656,508, issued Oct. 20, 1953, with the teachings of Richard G. Sweet in Report SEL-64-004 of the Stanford Electronics Laboratories, of Stanford University, published March 1964 and also identified as Technical Report No. 1722-1 prepared under U.S. Signal Corps contract.

The teachings of Coulter Patent 2,656,508 of interest to the present invention is the provision of a short dielectric duct or aperture of appropriate cross section through which the suspension fluid is forced to flow, and a pair of electrodes disposed on opposite ends of the aperture in contact with the fluid. The electrical resistance between the electrodes is affected by the presence and size of a particle in the fluid within the duct.

The teachings of Sweet (SEL-64-004) applicable to the present invention are the provision of an orifice through which the fluid is caused to flow and the application of vibration to the orifice which causes the fluid jet issuing therefrom to separate into discrete, equal volume droplets. Electrostatic droplet charging means are associated with the jet close to and downstream from the orifice where the jet separates into droplets to impose an electric charge on each droplet. Fixed potential electrostatic deflecting means downstream of the droplet charging means causes each droplet to deflect an amount related to the charge on the droplet.

In FIGURE 1 I have illustrated, in diagrammatic and block form, the combination of elements which form one practical embodiment of my invention. Liquid containing particles is suspension are stored in any suitable container **11**. Means for pressurizing the fluid may be any suitable method such as a pump in the outlet of container **11**, or gas pressure means **13** and controllable pressure reducing means **15**.

The fluid container **11** is connected by a strainer **17** and pipe **19** to nozzle **21**. Strainer **17** is provided to pass particles within the range of interest and to stop particles of gross size from clogging the system. Although the fluid in passing through the nozzle may be jetted and separated into droplets by suitably vibrating the nozzle, I prefer to apply pulsations directly to the fluid and avoid vibration of the nozzle. I accomplish this method of drop formation by resilient acoustic insulation **20** between nozzle **21** and acoustic coupler **23**. The acoustic coupler **23** is directly driven by an electrically driven vibrator such as piezoelectric driver **25** which in turn is energized by adjustable frequency generator **27**.

The frequency and amplitude of the output of generator **27** is correlated with the viscosity and velocity of fluid passing through the nozzle in order to produce equal size discrete droplets from the resulting jet.

Referring to FIGURES 1 and 2, sensor element **29** is shown associated with the fluid-containing system, preferably at the outlet of the nozzle. At the outlet of the nozzle the fluid has obtained its jet cross section and velocity so that the transport time between the passage of the fluid through the sensor and the point along the path of break-up of the jet into droplets is a fixed and calculable quantity.

The sensor **29** is selected to be responsive to the particular characteristic of the particles of interest, that is, it will be responsive to particle size, radioactivity, fluorescence, luminescence, electrical conductivity, light transmissibility, light reflectivity of any other characteristic which is capable of transformation into an electrical quantity.

The electrical pulse generated in the sensor by the passage of a particle is amplified and shaped by proportional pulse generator **31**. The utilization of the pulse to deflect the associated droplet is delayed an amount of time equal to the time consumed by the fluid containing the particle in traversing the distance from the sensor to the point where the liquid is detaching from the jet as a droplet. The pulse after appropriate delay in delay element **33** controls the amplitude and time of generation of droplet charging potentials. More specifically, each droplet or a group of droplets is charged by collar pulse generator **35** in response to the delayed pulse from delay element **33**. The collar pulse generator **35** produces the proper potential which is inductively impressed along the jet stream between charging collar **37** and sensor **29**. The charging collar surrounds the jet stream at a location which includes the droplet separation zone. Thus, the potential which exists between the collar and the sensor at the time of separation of the droplet, determines the bound charge on the droplet. The droplet, or train of droplets, continues in the direction of the jet stream until it passes between deflecting plates **39** and **41**. Deflecting plates **39** and **41** are energized with a steady state potential of suitable magnitude. Each droplet in passing between the deflection plates is deflected an amount determined by the charge on the droplet. The droplets are thus segregated in accordance with the amount of a selected characteristic and can be collected in any desirable manner. FIGURE 2 shows collection in ten catch basins but in some cases it is desirable to collect the segregated droplets on a moving strip of blotting paper. The element **43** in FIGURES 1 and 2 is intended to illustrate in general such various types of collection systems.

The system of FIGURE 1 is a simplified system illustrated to show generally the manner of accomplishment of the objectives of this invention.

The particle responsive sensor **29** is selected to generate an electrical quantity in response to a selected characteristic. Where sorting and collection in accordance with the presence of and size of particles is desired, the sensor preferably takes on the form of FIGURE 3. The sensor comprises the metallic end of nozzle **21**, a plate of dielectric material **22** and an end electrode **24**. Particles passing through the aperture in dielectric plate **22** cause a change in electrical resistance between nozzle body **21** and end electrode **24**. This change in resistance is transformed into an electrical pulse in proportional pulse generator **31** as described with reference to FIGURE 1.

In the separation of blood cells, a typical set of conditions is as follows:

Nozzle dielectric **22** aperture	microns	42
Electrode **24** aperture	do	36
Frequency of acoustic driver	kilocycles	72
Fluid (saline solution)	percent	0.9
Fluid pressure	p.s.i.	53
Transit time sensor **29** to collar **37**	microseconds	200
Duration of charging pulse on collar	do	200
Velocity of jet	meters/sec	14.6
Size of human red cell	cubic microns	85
Size of mouse red cell	do	42

The concentration of the blood cells in the saline solution is preferably maintained so that not more than one cell will appear in several, i.e., for example, seven droplets. The collar pulse is of a duration to impress an identical charge on each droplet in the sequence of seven. Although it would be preferable to treat each droplet separately, thus enabling a faster separation of particles from a more concentrated solution, the velocity across the cross section of the nozzle is not so uniform as to result in complete assurance that a detected particle will always appear in a certain droplet instead of the next droplet following. In the interest of reliability in sorting, a dilute solution is preferred and the collar charging pulse preferably brackets one or more droplets ahead and behind the droplet expected to contain the particle.

As is shown in FIGURE 3, the mass of the nozzle is eliminated from the vibratory system by acoustic insulators **45–47**. The effect of this is a reduction in demand on the acoustic driver and considerably greater effectiveness of the vibratory energy in "breaking up" the jet into uniform droplets. In addition, interference with clean application of the acoustic vibration to the fluid by the inertia of the nozzle mass and consequent multiple moding is avoided.

The improved nozzle of the present invention comprises a nozzle proper **21**, preferably of platinum. Acoustic coupling rod **23** is resiliently isolated from both the nozzle **21** and the housing **49** of the nozzle assembly by resilient O-rings **45** and **47**. The nozzle housing **49** includes the synthetic plastic shell **51** which contains a cylindrical bore in which the nozzle body **21** is preferably a slight squeeze fit. The nozzle is anchored in shell **51** by any convenient means such as cast-in-situ synthetic resin **53**. Both the nozzle and the shell **51** are provided with annular grooves to permit resin **53** to permanently lock the two in assembled relation.

The acoustic driver rod at its end portion has a diameter equal substantially to the largest diameter of the tapered nozzle **21**. The diameter of the driver end portion is reduced from that of the remainder of the driver rod for a distance adequate to accommodate O-ring **47**. The end portion of the drive rod is thus hydraulically sealed to the large end of nozzle **21** by O-ring **47**. The drive rod **23** is also provided with an integral enlarged portion **52** in order to provide a shoulder for O-ring **45** to bear against. Annular collar **54** provides a shoulder **55** for holding the assembly together with O-rings **45** and **47** under appropriate pressure when upper body member **57** is threaded onto body member **51**. Fluid duct **19** is inserted into nozzle **21** with a hermetically tight fit.

It follows that acoustic drive rod **23** is substantially a free piston as far as any part of the nozzle or nozzle assembly is concerned.

As mentioned above, although particle separation by size is important, other types of sensing are also possible and important. FIGURE 4 shows one form of sensor which is luminescent responsive. A light source **60** capable of emitting light of the selected frequency is coupled to the fluid duct by transparent window **61**. Particles which luminesce will emit light shortly after excited and will be detected by photocell detector **63**. The output of detector **63** is utilized as indicated in FIGURE 1.

FIGURE 5 schematically shows a sensor **29** to detect radioactive particles such as thyroid cancer cells. A scintillation element **69** is supported in cylinder **67** and in the path of pick-up of photo-sensitive assembly **63**. Numerous other types of sensors may be used, the only requirement being that the particle characteristic of interest be translatable into an electrical quantity by any of the methods known in the art.

Referring to FIGURES 6, 7 and 8 a complete electronic control system for association with the particle sensor and droplet charging system is shown. This system amplifies the pulses generated by particles passing through the sensor **29**, converts the pulse height information into digital form, stores the digital information in storage flip-flops and after a time delay equal to the transit time of the liquid in passing from the sensor to the charging collar, develops a pulse having a width tailored to the number of droplets in each group and the amplitude of which is determined by the stored digital information.

The electronic system contains (1) numerical logics which is concerned with the conversion of the digital information from analogue-to-digital converter **101** into a charging collar potential of corresponding magnitude, and (2) control logics which is concerned with the sequence of operation of the numerical information system.

The description of the electronic system to follow below will be more easily understood if the requirements of the system are first outlined.

The system is not to respond to particles having the characteristic of interest below a selected level. This is accomplished by lower boundary, or threshold discriminator **118**.

All particles or multiple particles causing a sensor response in excess of a selected range are to be segregated in a maximum throw collector. This is accomplished by upper boundary discriminator **119**. An output from this discriminator results in a maximum available collar charging potential in order to kick such particles into an end basin.

There is a certain time lapse between the time a particle causes a sensor signal and the time at which the same particle in a droplet separates from the jet. This time lapse produces two requirements, one of which is the storage of the digital output of the analogue-to-digital converter **101** until the information can be used, and the second requirement is the provision of an accurate time lapse control. The first requirement is met by an information storage system, which in this selected embodiment are storage flip-flops **103**. The second requirement is met by the provision of charging delay univibrator **157** (FIG. 7).

The collar charging potential must be the correct value corresponding to the magnitude of the particle characteristic of interest. This is accomplished by processing the output of analogue-to-digital converter **101** through storage flip-flops **103**, through binary-coded-decimal to decimal converter **129**, through charging pulse forming network **132** and digital-to-analogue converter **135**.

The charging collar potential for each droplet containing a particle must exit long enough for a droplet to be charged. This requires that the pulse be a rectangular pulse of correct length. This duration is obtained by charging time univibrator **159** which triggers-on for the correct duration the appropriate "and" circuit in the pulse forming network **132**. This in turn results in the correct rectangular pulse at terminal **147** (FIGURE 8) in the emitter-follower circuit of transistor **143**.

The output of sensor **29** is fed into pulse generator **31** and from there to the input of analogue-to-digital converter **101**. The capacity of the analogue-to-digital converter (multi-channel analyzer) is chosen to accord with the selected number of separations desired. Each digit is encoded into a 1–2–4–8 decimal code. In the embodiment herein described, the particles are to be collected in ten catch basins **43**, and because for purposes of convenience, an analogue-to-digital converter of 100 channels was used, only the tens of the address are used.

The tens pulses of the address are current amplified in emitter followers **104–107** and pass through "and" gates **111–117** which are inhibited if the pulse from the sensor **29** is greater than the selected upper limit set by upper discriminator **119**. However, a pulse from upper discriminator **119** is used to deflect an oversize particle into the "ten" basin (see FIGURE 2). To this end, the upper discriminator pulse is shaped in Schmitt trigger **144**, generates a negative pulse of approximately 85 microseconds in duration in univibrator **127** which inhibits "and" circuits **111–117** but also directly activates "or" circuits **121** and **123** which inserts the 8 and 2 bits into storage flip-flops **103–B** and **103–D** through "and" circuits **125–B** and **125–D**.

The upper discriminator pulse also passes through "or" circuit **128** and after a 5 microsecond delay generates a 5 microsecond transfer pulse which inserts the ten into the storage flip-flops which, as will be seen later, results in the application of a voltage to the charging collar of magnitude in excess of that selected for segregation of particles in the lower ranges of interest.

If the sensor **29** has detected a particle which, for example, is to be collected in the third catch basin of FIGURE 2, two signals are originated. The lower discriminator **118** delivers an activation pulse which travels along line A to Schmitt trigger **148** (FIGURE 7). The same

signal is converted in analogue-to-digital converter **101** into a "3" which is a positive output on the "10" and "20" addresses. These "ones" pass through emitter followers **104** and **105** to "and" gates **111** and **113**. These "and" gates are not inhibited by the presence of an upper bound pulse and therefore insert "ones" through "and" gates **125–A** and **125–B** into the storage system **103**. The analogue-to-digital converter upon completion of a count also generates an add-1 pulse. This pulse triggers Schmitt trigger **155** which delivers a pulse through "or" circuit **128** to transfer delay circuit **130** which after a 5 microsecond delay triggers transfer-pulse-generator **131** which generates a 5 microsecond long positive square transfer pulse.

The occurrence of the transfer pulse on "and" circuits **125–A** to **125–D**, together with "ones" from the analogue-to-digital converter on **125–A** and **125–B**, causes a positive pulse to appear on the output of the flip-flops **103–A** and **103–B**. The flip-flops and emitter followers in the output of the flip-flops are arranged so that a "1" is negative and a "0" is positive. Therefore, a "1" on the input of flip-flops **103–A** and **103–B** and a "0" on the input of flip-flops **103–C** and **103–D** gives rise to the following conditions on terminals E to L: a negative voltage on F, H, I and K and positive voltages on E, G, J and L. There are, therefore, plus voltages on buses 1, 2, $\overline{4}$ and $\overline{8}$ of the binary-coded-decimal to decimal converter **129**. These simultaneous positive voltages cause a plus output from "and" circuit **131–C**. The plus potential remains on the output of the "and" circuit **131–C** until an enabling signal is put on line D.

The generation of the enabling "pass" signal on line D takes place in the apparatus of FIGURE 7. The signal pulse from the lower discriminator passes through normally enabled "and" gate **153**. This pulse triggers charging delay generator **157**. Charging delay generator **157** delivers a block-out triggering pulse **154** to cause block-out "or" gate **155** to start the block-out pulse. At the end of the delay time set in charging delay generator **157** a triggering pulse is generated to trigger charging time generator **159**. The output of charging time generator **159** also goes into the input of "or" circuit **155** so that a block-out or inhibiting potential is applied to "and" gate **153** from just after time to start signal on line A is received until the corresponding droplet is separated from the jet. The output pulse from the charging time generator, together with the add–1 pulse, passes through "and" circuit **152** and alters the state of flip-flop **154**. The output of flip-flop **154** passes a pulse onto line D when "and" gate **161** is "enabled" by the output pulse from charging time generator **159**, and only during such time of enabling. The next pulse from the lower discriminator resets flip-flop **154**.

The occurrence of the steady state potential on the D line (FIG. 8) enables the appropriate "and" gate in the charging pulse formation network **132** to pass the output of the activated one of gates **131–A** to **131–J** to the digital-to-analogue converter **135**. In the example herein treated, "and" gate **131–C** is enabled by the potential on line D to pass a pulse through its emitter follower to input (3) which open-circuits transistor **135–C**. This permits the 90 volt potential on the collector of transistor **135–C** to raise the base potential of output transistor **143**. The resistor string **149–A** to **149–K** is proportioned so that the output voltage on terminal **147** has a value of 90 volts.

It was stated supra that an outsize particle resulted in a maximum collar potential at terminal **147**. The signal from upper discriminator **119**, after processing by Schmitt trigger **144** (FIG. 6) and in univibrator **127** generates an inhibt potential on "and" circuits **111** to **117** and goes through "or" circuits **121** and **123**. Therefore, flip-flops **103–B** and **103–D** are switched. Therefore, negative potentials appear on terminals E, H, I and L and positive potentials appear on F, G, J and K. Referring to FIG-

URE 8 it is seen that buses $\bar{1}$, $\bar{4}$, 2 and 8 of the binary-coded-decimal to decimal converter carry positive potentials and that "and" circuit 131–J is the only "and" circuit enabled. This in turn triggers-off transistor 135–J and results in 300 volts approximately on terminal 147.

The construction and operation of the digital-to-analogue converter 135 is now described. Each transistor 135–A to 135–J is connected through its respective collector resistor 134–A to 134–J to a 600 volt potential source through a string of voltage dividing resistors 149–A to 149–J. The values of the dropping resistors were chosen in this example to provide supply voltages to the cathodes of diodes 137–A to 137–J which increase by 30 volt increments. Thus a decoded "1" goes to transistor 135–A with a 30 volt supply, and a decoded "10" goes to transistor 135–J with a 300 volt supply.

With no inputs, all of transistors 135–A to 135–J are "on" and in a saturated condition so that the collectors are at less than one volt above ground. When a negative pulse is received it applies a reverse bias to the base-emitter junction of the corresponding transistor which turns the transistor off. As the collector current falls to zero, the voltage on the collector charges up to the voltage on the supply voltage resistor divider string and passes through the respective diode (137–A–137–J) to the base of emitter follower 143. The voltage pulse appearing on the emitter of emitter follower 143 is applied to charging collar 37.

The particular electronic system above described is presented only for purposes of illustrating a complete embodiment and not in any limiting sense. Any other electronic system capable of performing the desired functions may be used.

What is claimed is:

1. Apparatus for separating small particles suspended in a fluid in accordance with the amount of a selected characteristic of each particle comprising means for jetting the fluid, sensor means surrounding the path of the fluid jet for generating an analogue electrical quantity in response to the passage of a particle, means for acoustically pulsing the fluid jet to cause separation into droplets in a discrete separation zone, electrical charging means surrounding the jet path at the separation zone, electrical delay and charging means connected between said sensor and said electrical charging means having a period of delay equal to the time of passage of a particle passing from the sensor means to the droplet separation zone, electrical deflecting means supported symmetrically about the path of the droplets, whereby each droplet containing a particle is deflected an amount corresponding to the amount of characteristic of the particle contained therein.

2. A device for sorting minute particles suspended in a fluid comprising a nozzle for jetting the fluid, a particle sensor supported adjacent the outlet of the nozzle for generating an electrical quantity in response to a selected characteristic of a passing particle, means for acoustically pulsing the fluid jet in the direction of its motion whereby the jet separates into droplets in a fixed zone, a conducting charging collar surrounding the jet and supported to surround the zone of droplet separation, electrical charging means connected through electrical delay means to the particle sensor to develop a collar charging potential having a magnitude related to the magnitude of output of the sensor, said electrical delay means electrically connected between the sensor and the electrical charging means having a delay period equal to the transport lapse time of fluid passing from the sensor to the zone of droplet separation whereby each droplet containing a particle is impressed with a bound charge having a magnitude related to the magnitude of the characteristic of the particle in the droplet, a pair of electrical deflecting plates supported symmetrically about the train of droplets down stream of the charging collar whereby each droplet is deflected an amount proportional to the amount of characteristic of the particle contained in the droplet, and catch basins support in a plane normal to the jet path for collecting the segregated particles.

3. Apparatus for sorting minute particles suspended in a fluid comprising, a nozzle for jetting the fluid, means supported on the nozzle for acoustically pulsing the fluid passing therethrough, a particle sensor consisting of a pair of electrodes spaced by a dielectric separator supported on the outlet end of said nozzle, said electrodes and said dielectric separator each containing a central aperture having a diameter adapted to pass with slight clearance the largest particle of interest and said electrodes and dielectric separator being supported with their apertures aligned with one another, means for impressing a potential across said electrodes whereby each particle passing through the apertures generates an electrical quantity, said electrodes being connected to a multi-channel analogue-to-digital converter having digital outputs and an add-1 pulse output, electrical memory storage means connected to the digital output of the analogue-to-digital converter, electrical delay means having a selected time constant connected between the analogue-to-digital converter add-1 output and the memory storage means for transferring to output terminals the content of the storage means at the end of the selected time constant, means electrically connecting the output of the memory storage means to a binary-coded-decimal-to-decimal converter and means electrically coupling the output of the binary-coded-decimal-to-decimal converter to a digital-to-analogue converter whereby decimally related potentials are generated in the output of the digital-to-analogue converter corresponding to ranges of particle sizes, a cylindrical metal charging collar supported colinearly with the nozzle at the zone of separation of the jet into droplets, said electrical delay means selected time constant being equal substantially to the duration of time consumed by fluid in passing from the sensor to the droplet separation zone, said charging collar being electrically connected to the output of the digital-to-analogue converter, electrical charge deflecting means supported symmetrically about the axis of the nozzle and down stream of the charging collar and a plurality of droplet collection basins supported below the deflection means and along a path normal to the nozzle axis.

References Cited

UNITED STATES PATENTS

2,646,880	7/1953	Frankel	209—111.6
2,656,508	10/1953	Coulter	324—71
2,756,388	7/1956	McLean	324—32
3,123,541	3/1964	Donnell.	
3,124,172	3/1964	Paxson.	

FRANK W. LUTTER, *Primary Examiner.*