

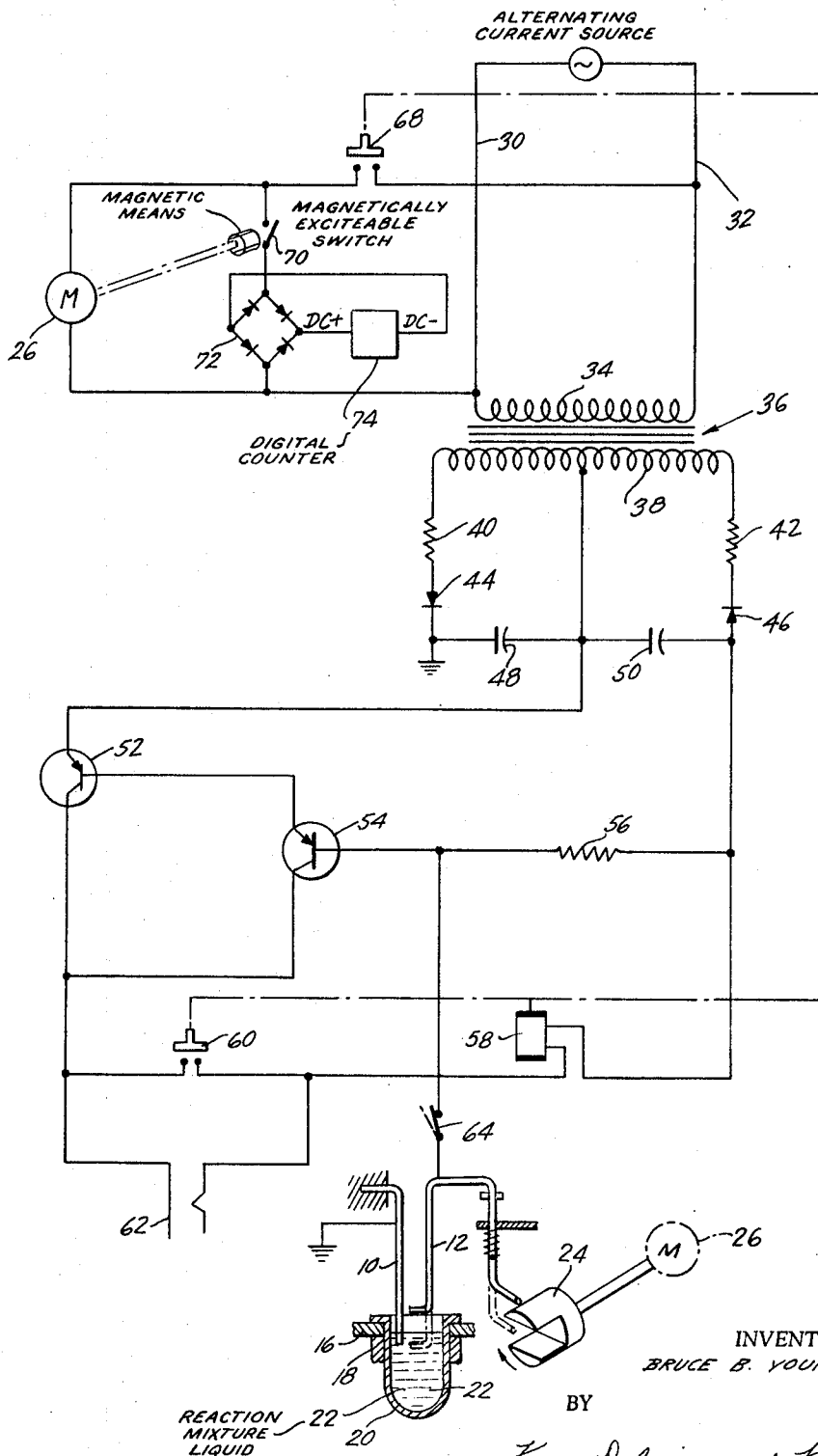
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ELECTRICAL APPARATUS FOR FIBER DETECTION

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ELECTRICAL APPARATUS FOR
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This invention relates to electrical conductivity detection apparatus and, more particularly, to a system for detecting the presence of a particular resistive medium in liquids.

There are a number of applications in which it is desirable to detect the presence of an electrical resistive body of rather minute dimensional proportions. For example, the presence of fibers or similar structural members in liquid or the initiation of fibrillation therein, in many fields, may be a critical factor. The formation of fibers is extremely significant in blood coagulation. In this connection, the clotting capabilities of a patient's blood, its characteristics and clotting times and the hemotosis mechanism in general have an important bearing in surgery and therapy. With this in mind, the coagulation properties of blood plasmas are ordinarily measured for such in diagnostic and therapy control. It has been proposed that such measurements be made in terms of time. That is the time in which liquid blood transforms into a semi-solid gel-like state of consistency.

In particular, the hemotosis mechanism is evaluated in many instances by prothrombin time determinations. Prothrombin time is defined as the period required for a particular specimen of prothrombin to induce blood plasma clotting under standardized conditions in comparison with normal human blood. With respect to the latter the time is usually between 11.5 and 12 seconds. If there is a departure, either a faulty technique or mechanism is involved.

Clotting is essentially a function of the plasma and involves the changing of one of the plasma proteins, fibrinogen, from the sol (liquid) to the gel (solid) state. The change in consistency is brought about by tiny, threadlike insoluble structures in which form an interlacing network of fibers, made of a protein called fibrin.

The clotting processes are initiated and accelerated by the juices from injured tissues. Both injured tissues and disintegrating blood platelets give off similar substances, collectively thrombokinasase, which initiate the clotting reaction. Clotting, thusly occurs automatically at the proper time. When blood escapes from an injured vessel it is immediately exposed to juices from damaged tissue and its platelets disintegrate releasing additional thrombokinasase.

Thrombin is the immediate factor in the mechanism which changes fibrinogen into fibrin and produces the clot. Thrombin exists in the blood in an inactive form, prothrombin, which is changed by thrombokinasase and calcium into thrombin at the time of clotting. Prothrombin itself does not occur as such in normal plasma, but is combined with a substance called anti-prothrombin, with which thrombokinasase is united in order to initiate the clotting mechanisms. This union releases the prothrombin. This prothrombin is changed into thrombin by the presence of calcium. The thrombin together with fibrinogen, the soluble protein present in normal plasma, produce fibrin, the insoluble protein which constitute the actual clot.

In accordance with a particular proposed technique for medical as well as clinical use, standardized and stabilized chemical reagents are placed in tubes and heated to normal body temperatures, notably 37° C. the accepted

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standard. Ordinarily, a reagent will include various activators for causing plasma to experience thrombosis. Such activators may include thromboplastin and calcium ions. Reagents of this type are available commercially as for example, Calsoplastin, a reagent composed essentially of thromboplastin extract with calcium chloride added. The quantity of reagents is ordinarily fixed for proper prothrombin time determinations. With this in mind, controlled plasma at the standard operating temperature and of the predetermined quantity also in tubes, is then dispensed in one of the tubes containing reagent. A probe is then inserted and withdrawn from the reaction mixture for purposes of sensing the initial clot formation. This operation is also conducted at the standard operating temperature. The same procedure is followed utilizing a controlled amount of patient's plasma. The prothrombin times are read and recorded.

Quite obviously, unless this procedure is controlled and accurately conducted inaccurate and erroneous results are inevitable. Under such circumstances, this may reflect in improper therapy administration. Unless, conducted efficiently and expeditiously in case of emergencies, errors will be compounded and multiplied.

It is therefore, a principle object of this invention to eliminate the drawbacks and disadvantages mentioned in the above and at the same time provide for accurate, automatic means for sensing and detecting the presence of a particular resistive medium in liquids.

Another object is to provide for such sensing means, together with positive indication and recordation of the time factor for completing this determination.

A further object is to provide highly sensitive, electrical circuitry for detecting the initiation of fiber formation incident to fibrillation.

An important object is to provide for the above in prothrombin and coagulation time determinations and in measurements of the coagulation properties of blood and blood plasma.

Although the present invention has wider application in measuring the properties of liquids or the detection of particular materials therein, the disclosure will be devoted primarily to prothrombin time determinations. It should be understood, however, that the invention is not to be construed as being limited thereby because of the contemplated broad applications.

With this in mind, the present invention briefly stated includes a Darlington coupling of transistors having their respective collectors tied directly to one another. This coupling has the effect of permitting the transistors to perform substantially as if only a single transistor were present but permits greater current gain. In this connection, the higher current gain is advantageously utilized to drive a relay. At the same time, however, this transistor coupling provides a smaller current through detecting probes.

These probes are employed in detecting the presence of a particular medium or the initiation of fibrillation in the selected liquid. One of the probes is movable, whereas the other is stationary. The movable probe is inserted into and removed from the liquid in a timed sequence. The low current is only adapted to flow through the probes when the movable probe is elevated above the surface of the liquid. Under such circumstances, when a fiber or more than one adheres to this probe and at the same time extends into the liquid, a circuit is completed. When the resistance of the fiber is detected the transistors are placed in a non-conducting state so as to de-energize the relay, which, in turn, serves to stop the running of the timer. The time for fibrillation is then recorded.

The movable probe is automatically operated and is driven by a motor. A complete cycle into and out of the

liquid material traverses in the case of prothrombin time determinations, approximately two cycles per second. The motor additionally serve to rotate a magnet which is adapted to pass in close proximity to a magnetically excitable switch during each revolution. In this manner, an electrical pulse is generated which energizes a counter, thereby recording time. Thus pulsing is variable and in the above specific application may be every tenth of a second. The circuit for both the timer and probes is closed deliberately and automatically opened upon detection of a resistive fiber of the liquid.

Other objects and advantages will become apparent from the following detailed description which should be taken in conjunction with the accompanying drawing, illustrating a somewhat preferred embodiment of the invention and in which the sole figure is a diagrammatic view of electrical circuitry incorporating the teachings of the present invention shown in association with stationary and movable probes in a reaction mixture in a tube, all of which are supported by a frame shown fragmentarily.

In the figure a pair of probes 10 and 12 are shown disposed above frame 16. Probe 10 is stationary and electrically grounded, whereas probe 12 is movable. Frame 16 may conveniently mount the components of the electrical circuitry of this invention and may include a heating block having coupled thereto suitable heaters and thermostats for maintaining standard operating temperatures as is preferably the case in blood plasma prothrombin time determinations. The frame 16 may, additionally, include a reaction well 18 adapted to advantageously receive a tube 20 for containing the reaction mixture or liquid to experience fibrillation. The probe 12 is preferably movable in a substantially vertical path or sweep in order that it may be immersed in the liquid 22 and then removed to complete a single cycle. In time, this probe 12 will eventually have one or more fibers clinging thereto when elevated and at the same time suspended in the liquid 22 to complete an electrical circuit between the probes.

The movable probe, as shown, rests on a stepped cam 24 which is adapted to raise the movable probe 12 and then lower it into the liquid 22 twice each cam revolution. This cam 24 is fixed to the output shaft of motor 26 which is a constant speed motor adapted to rotate its output shaft at a rate of one revolution per second. Motor 26 is a single unit though shown twice in the drawings. It should be understood, that the rate in which the movable probe is raised and lowered, the configuration of the cam 24 and the characteristics of the output of its motor 26, particularly, may be varied depending upon the liquid to be tested for fibrillation. Furthermore, although in this disclosure the specific embodiment is directed to the application of fibrillation detection.

Referring now to the remainder of the circuitry illustrated, leads 30 and 32 extend to the selected electrical energy source and may include suitably rated fuses. These leads are connected to the primary winding 34 of step-down transformer 36. The secondary winding 38 of this transformer is coupled with resistors 40 and 42. A rectifying diode 44 is connected with resistor 40 and then to chassis ground, as shown. The resistor 42 is likewise connected with a diode 46 which, in turn, is connected between the junction of diode 44 and ground and, at the same time, with the center-tap of the transformer 38. Filtering capacitors 48 and 50 are interposed at each side of this connection with the center tap. The center tap of the transformer 38 is then coupled with the emitter of the transistor 52 forming part of a Darlington coupling in which transistor 54 is included. The collectors of these transistors in this coupling are tied directly to one another, as shown, whereas, the base of transistor 52 is connected with the emitter of transistor 54. The base of transistor 54 is connected with the diode 46 through inter-

posed resistor 56. The junction between this resistor 56 and diode 46 is connected to one side of relay 58. The other side of this relay 58 is connected to the junction of the transistor collectors through its normally opened switch 60.

It should be understood that the coupling of the transistors 52 and 54 with their collectors tied directly to one another permits them to perform essentially as a single transistor but with greater current gain. This higher current gain provides an adequate drive for the relay 58 while, at the same time, provides for a smaller current through the probes. By having a greater current to the relay, it is possible to use a less sensitive and hence a less expensive relay.

A jack 62 is connected across the switch 60 and may be employed to connect the circuit to an externally located switch for manually or, for that matter, automatically energizing the circuit. In this manner, the relay switch 60 may be by-passed.

The junction between resistor 56 and the base of transistor 54 is electrically connected with the movable probe 12. A switch 64 may be interposed between this connection. This switch 64 is actuated by the operation of the output shaft of motor 26. Accordingly, the opening and closing of the switch 64 will be synchronized with the vertical movement of the movable probe 12. This can be accomplished through the operation of cam 24 if desired. Thus, when concerned with fibrillation applications, the circuit between the movable and stationary probes 12 and 10 will be open when the movable probe 12 is lowered into the liquid or reaction mixture 22 but will close when the probe 12 is raised from the liquid 22. Under such circumstances, a circuit will be completed between the probes only at such time as an electrical conductive fiber is lifted by the movable probe 12 from the liquid 22.

Referring now to the motor and timer circuit of this invention, it will be observed that this circuit is connected across the leads 30 and 32 and is adapted to be opened and closed by means of the switch 68. This switch, as well as switch 60, is adapted to be manually closed and then held in a closed position by the energization of its relay 58. As will be explained in detail shortly, when a fiber is detected by the movable probe 12, the circuit to the relay 58 is shorted, thereby resulting in its de-energization. Consequently, the switches 60 and 68 will open. The motor 26 is included in this circuit and is series connected with the switch 68. Connected across the motor 26 and in series with the switch 68 is a reed switch 70 which is adapted to close by means of the magnet revolvable with the output shaft of the motor 26. For purposes of the present discussion, the magnet, through a suitable gear network will revolve at a rate ten times faster than the motor output shaft thereby closing the switch 70 every tenth of a second. This switch 70 is connected to one side of a diode bridge rectifier 72, both of which are connected across the motor 26. The signal rectified by the diode bridge 72 serves to actuate the drive of a digital counter 74 which will record each pulse received incident to the closing of the reed switch 70. Such digital computers or digital counters are well known and commercially available.

In the operation of the present invention, the electrical leads 30 and 32 are connected with the electrical energy source. The tube 20 is then placed in the reaction well 18 of the test unit 16 and is then provided with the reaction mixture liquid 22 to be subjected to fibrillation, with one or more of the constituents being already contained in the tube or dispensed therein to initiate the reaction. For example, the tube may initially contain the selected chemical reagent in measuring the coagulation properties of blood plasma. A predetermined dosage of blood plasma would then be inserted. The stationary probe 10 and movable probe 12 are immersed in the mixture 12 at the inception of the reaction or after a short

time delay if desired. Immediately thereafter, switch contacts 60 and 68 are simultaneously closed; at this time, the relay 58 is energized to maintain its switches 60 and 68 in a closed condition, thereby eliminating the need to manually maintain these switches in this position. The motor 26 will accordingly be actuated to impart rotation to its output shaft, and, consequently, to the driven magnet coupled therewith for rotation. Upon each traversal of the magnet past the reed switch 70, an electrical pulse will be rectified by the diode bridge 72 to actuate the counter 74. As stated, the pulsing of the counter may be selected to occur at tenth of a second intervals.

The center tap of the transformer 38, as well as the junction between capacitor 50 and diode 46, will be at nominal negative D.C. voltages with the voltage at the center tap being ordinarily less than that at the capacitor and diode junction. The motor 26, as stated, through the operation of the cam 24 will raise and lower the movable probe 12 out of and into the reaction mixture 22 at the selected and preset rate.

The cycle of movement of the movable probe 12 is predetermined and in the case of prothrombin time determinations may be at the rate of two cycles per second. In this connection, when the movable probe is immersed in the liquid 22 the switch contact 64 is opened so that the current path between probes through the liquid will not have an effect on the circuit. When the movable probe is elevated or raised above the liquid level the switch contact 64 closes. However, in view of the extremely highly resistant airgap between movable probe 12 and liquid 22 the transistors 52 and 54 are in a conducting state. Whenever the resistance measured across switch 64 and the probes 10 and 12 to ground exceeds the value of resistance 56, the voltage at the base of transistor 54 is more negative than the voltage at the emitter of transistor 52. This is because of the voltage dividing action of resistance 56 and the resistance across the probes 10 and 12, both of which are in series between the higher negative voltage and ground. Under this condition, transistors 52 and 54 are in the conducting state and current flows from the transformer center tap through the emitter and collector of the transistor 52, through the relay contact switch 60, the relay coil 58 and back to junction of capacitor 50 and diode 46. If the resistance across the probes 10 and 12 to ground becomes lower than resistance 56, as for example, when a fiber is lifted by the movable probe 12 from the liquid 22, the transistors 52 and 54 switch to the nonconducting state. In this connection, ground or a positive voltage will be applied to the base of the transistor 54. This bias serves to turn off the transistors. The relay 58 will, as a consequence, become de-energized opening its switch contacts 60 and 68 thereby stopping the operation of the motor 26. The counter 74 and movable probe 12 will cease operating. Accordingly, the time period in which the fibrillation process is initiated will be recorded.

In one illustrative embodiment applicable to prothrombin time determinations the following values for the various components of the circuit were found satisfactory.

Resistor:

40 ----- 47 Ω .
42 ----- 47 Ω .
56 ----- 510 K Ω .

Capacitor:

48 ----- 50 mfd.
50 ----- 50 mfd.

Diode:

44 ----- 1N34.
46 ----- 1N34.

Diode bridge rectifier 72, each

diode ----- 1N1693.

Transistor:

52 ----- 2N1372.

54 ----- 2N1373.

Motor 26 ----- "Synchron" motor, Hanson Mfg. Co.

5 Switch 70 ----- Magnetic Reed Switch, Hamlin.

Counter 74 ----- Veeder Root Counter, Veeder Root Mfg. Co.

Probes 10 and 12 -- Stainless Steel.

10 Transformer 36 -- With 115 v. applied across the primary at 50 to 60 c.p.s., designed to supply 32 v. at 10 ma. at two secondary end taps and after filtration by diodes 44 and 46, 50 ma. D.C. current. The voltage at the emitter of transistor 52 was -20 v. and at the junction of resistor 56 and diode 46 was -40 v.

Aliquots of plasma were blown into thromboplastin reagent and the switches 60 and 68 substantially simultaneously pressed to initiate the movement of the probe 12. The reaction well column was calibrated for approximately 0.3 ml. with 0.2 ml. for reagent plus 0.1 ml. for plasma. The probe movement was such as to duplicate manual techniques in that the electrode movement was identical to that of trained technicians using a wire loop. Thus, the guesswork in determining end points in the time determinations was eliminated. The moving electrode alternately descended and lifted to seek and sense initial clot formation. When the end point occurred, the moving electrode 12 and the timer stopped. The prothrombin time in seconds and 0.1 seconds were registered on the digital read out 74.

The stationary probe 10 and movable probe 12 were raised from the reaction well and placed in a rest position. The digital read out 74 was such that by merely depressing a reset button the counter was cleared. The electrodes 10 and 12 only required cleaning by wiping and were repositioned at rest in readiness for subsequent tests.

Thus the aforementioned objects and advantages are most effectively attained. Although a single somewhat preferred embodiment of the invention has been described and illustrated herein it should be understood that the invention is in no sense limited thereby and is to be determined by the scope of the appended claims.

I claim:

1. An electrical circuit for detecting the presence of fibrin in a blood specimen in prothrombin time determinations comprising: a pair of electrodes, one of said electrodes being movable into and out of said specimen and the other of said electrodes being stationary in said specimen, drive means for moving the movable electrode into and out of said specimen, first switch means in said circuit for permitting an electrical potential to be applied across said electrodes, synchronization means synchronized with the operation of said drive means for removing the electrical potential across said electrodes when said movable electrode is immersed in said specimen and for permitting the application of said electrical potential when said movable electrode is out of said specimen, said synchronization means including switch closing means for closing said switch upon lifting of fibrin from said specimen by the movable electrode to thereby provide a current path between said electrodes through the fibrin and specimen, and electrical means in response to said switch closing means for deactivating the operation of the drive means when the current path between said electrodes is so provided, a second switch means for energizing said drive means, magnetic means driven by said drive means, a magnetically excitable switch adapted to be closed upon each traversal of said magnetic means in close proximity thereto, a counter coupled with said magnetically excitable switch and adapted to register a digital amount upon each closure of said magnetically excitable switch.

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2. The invention in accordance with claim 1 wherein relay means are coupled with said first switch means and adapted to be energized upon closure of said first switch means and adapted to maintain said first switch means in a closed position, and means for de-energizing said relay means and consequently open said first switch means upon detection of the presence of fibrin in the blood specimen between said electrodes, a power supply section including a transformer, a pair of diodes coupled with the secondary of said transformer, surge limiting resistors in series with each of said diodes, and filter capacitors connected with one end of each of said diodes and to one another.

3. The invention in accordance with claim 1 wherein relay means are coupled with said first switch means and adapted to be energized upon closure of said first switch means and adapted to maintain said first switch means in a closed position, and means for de-energizing said relay means and consequently open said first switch means upon detection of the presence of fibrin in the blood specimen between said electrodes, and a pair of connected transistors in cascade having their collectors electrically tied to one another for providing sufficient current to drive said relay means.

4. The invention in accordance with claim 3 wherein one of said electrodes is movable, a resistance is coupled with the base of the second transistor in cascade, and said movable electrode is connected with the juncture of

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said resistance and the base of said second transistor, and when the current path between said electrodes is closed, said transistors switch to a non-conducting state thereby de-energizing said relay.

5. The invention in accordance with claim 1 wherein a diode bridge rectifier is in series with said magnetically excitable switch, and said diode bridge rectifier is coupled with said counter and adapted to supply a direct current pulse thereto upon each closure of said magnetically excitable switch.

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