Hemolysis Due to External Blood Circulation and its Effects on Conductivity

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External Blood Circulation

- Medical technique used when blood is transported to an external machine
- Takes over the function of an internal organ.
- Cardiopulmonary Bypass: Adds oxygen, removes carbon dioxide from your blood, pumps it back.[1]
- Dialysis: Clean waste and extra fluid from blood, returns clean blood to the body.[2]

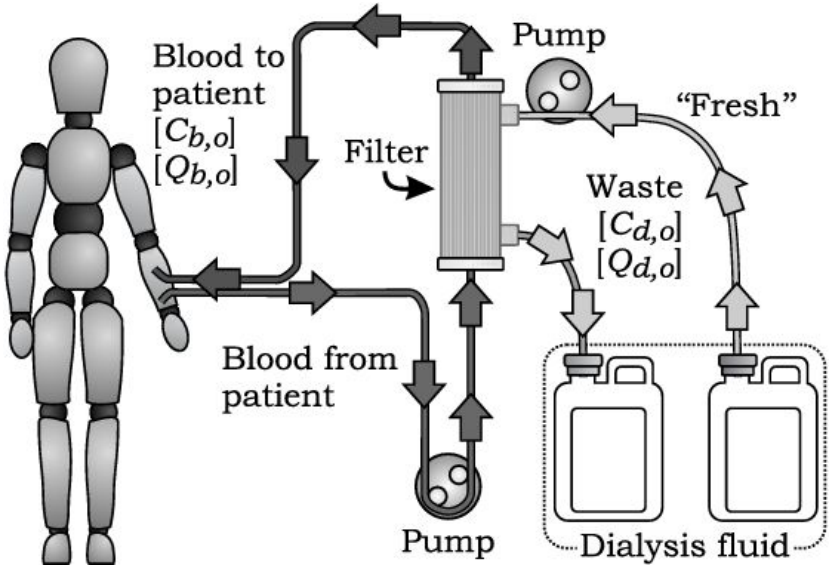


Figure 1: Diagram depicting the flow of blood in a dialysis machine [3]

Hemolysis

- Rupture of RBCs
- Hemoglobin released and decomposes
- A hemolysis rate of 2% or less is considered the benchmark of best practice by the American Society for Clinical Pathology.[4]

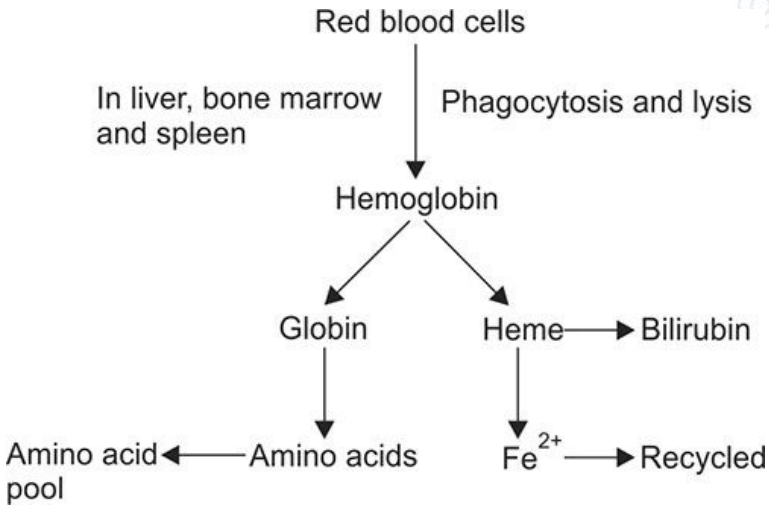


Figure 2: Diagram depicting the decomposition of hemoglobin.[5]

Symptoms of Hemolysis

- Extracellular (Free) Hemoglobin [18]
  - Acute and chronic vascular disease
  - Inflammation
  - Thrombosis
  - Renal failure
- Free Heme [19]
  - Endothelial cell injury
  - Vascular inflammatory disorders
  - Renal failure
  - Arteriosclerosis
  - Peritoneal endometriosis
  - Heart transplant failure.
- Hyperkalemia [6]
  - Muscle weakness
  - Numbness / tingling
  - Nausea / vomiting
  - Decreased reflexes
  - Paralysis
  - Respiratory failure
  - Arrhythmia
- Anemia [7]
  - Dyspnea
  - Fatigue
  - Muscle pain
  - Angina & heart attack
  - Chills/fever
  - Yellowing Skin
  - Dark Urine

Causes of Hemolysis

- Natural hemolysis occurs naturally in the spleen and liver.[8]
- Hemolysis can also be caused by mechanical trauma
  - External blood circulation machines [9]
  - Syringe sizes of less than 21 gauge [10]
  - Kinked blood lines [11]
- Intravascular hemolysis: cell destruction inside the veins, cell parts circulate
- Extravascular hemolysis: cell destruction outside the veins, such as in spleen [8]

Effects of Hemolysis on Blood

- Blood is naturally conductive
- Outer lipid bilayer
- Healthy RBCs do not impact overall conductivity.
- Hemoglobin and heme are both charged molecules
- Iron ions possess a charge
- Increase in conductivity of the entire fluid [12]

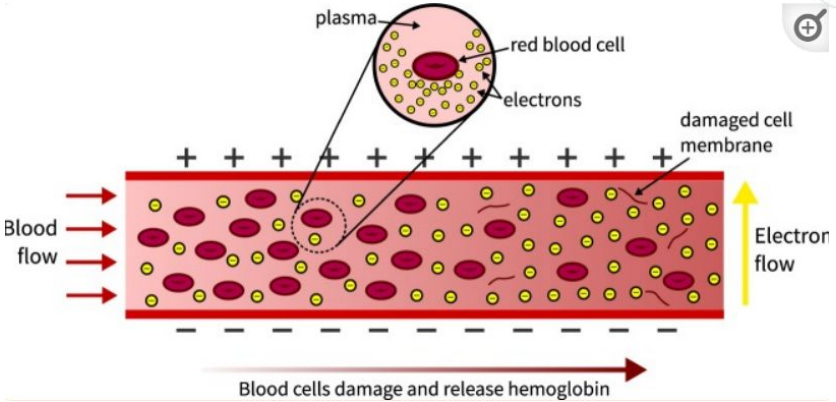


Figure 3: Simplified illustration of blood flow to show how hemolysis leads to a higher blood conductivity. [12]

Current Diagnosis Techniques

- Complete blood count (CBC), or other blood tests [13]
  - Decreased haptoglobin
  - Increased reticulocyte
  - Increased bilirubin
- Urine test [13]
  - Urobilinogen and hemoglobin in urine
- Bone marrow aspiration or biopsy
- Centrifugation and Spectrophotometry [12]

Natural Solutions to Hemolysis

- The spleen takes the old and damaged blood cells out of circulation from the bloodstream
  - 120 day cycle
- Bone marrow produces new blood cells [8]
- Scavenging molecules [14]

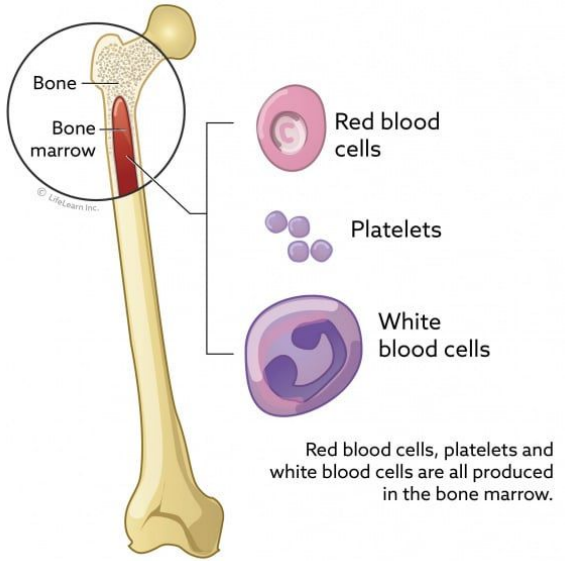


Figure 4: Bone marrow produces cells to replenish the healthy blood supply [15]

Scavenging Molecules

- Hemoglobin binds with Haptoglobin (Hp)
- Heme binds with Hemopexin (HPX) [14]
- Iron binds with Ferritin [16]
- No research of their effects on blood conductivity
  - Return to equilibrium should then lower conductivity

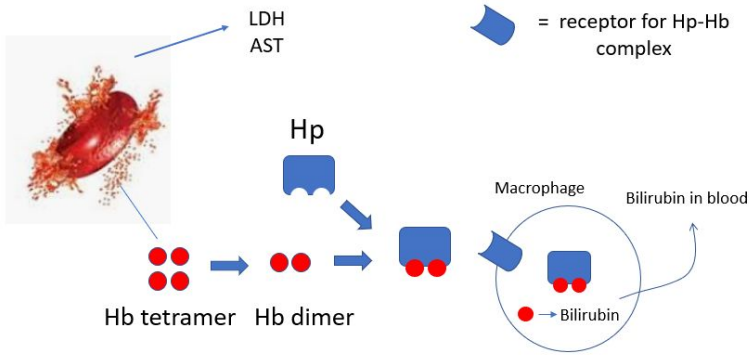


Figure 5: Example of Haptoglobin binding with hemoglobin. [17]

Goals of Design

- Measure resistivity of blood to determine % hemolysis
- Use this % hemolysis to dispense a certain amount of scavenging molecules into the blood
- Allow a buffer of 0-2% hemolysis without activation of the pump
- Return to homeostasis should have a negative feedback loop on the amount dispensed
  - It is presumed that the scavenging molecules neutralize the charge in blood

Hemolysis and Resistivity / Conductivity

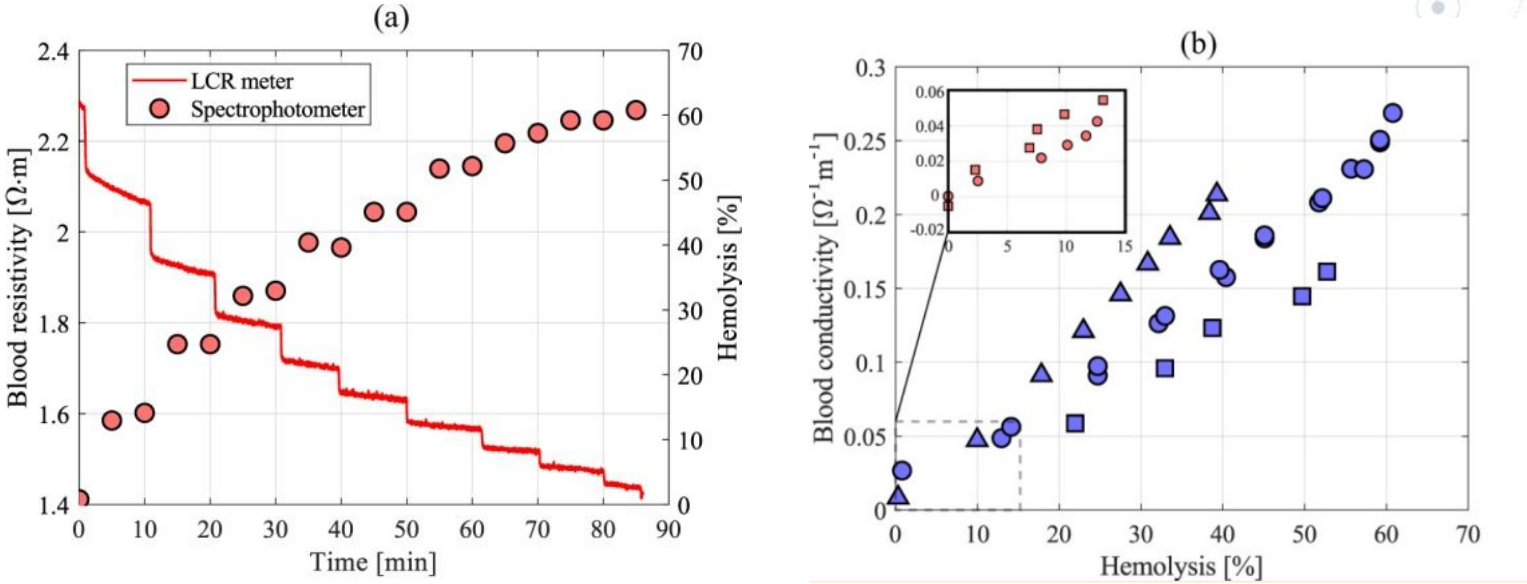
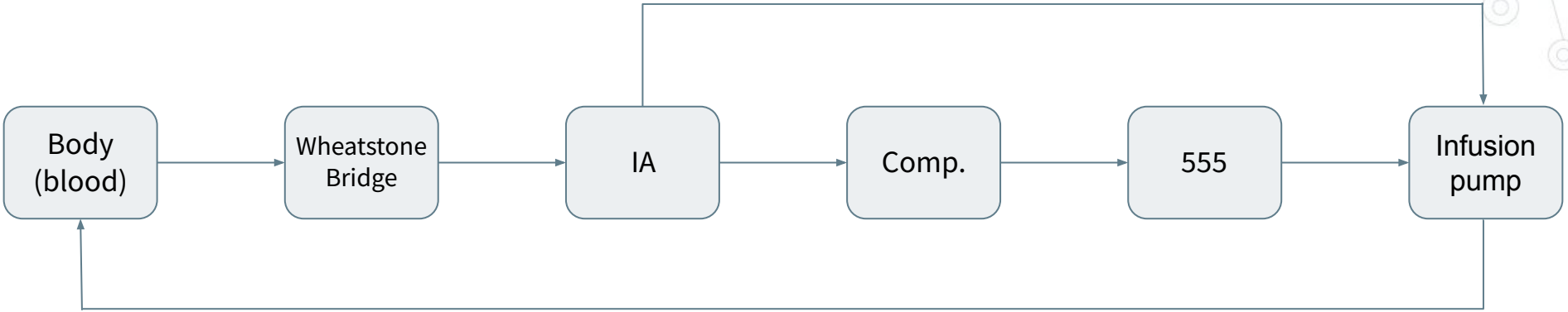
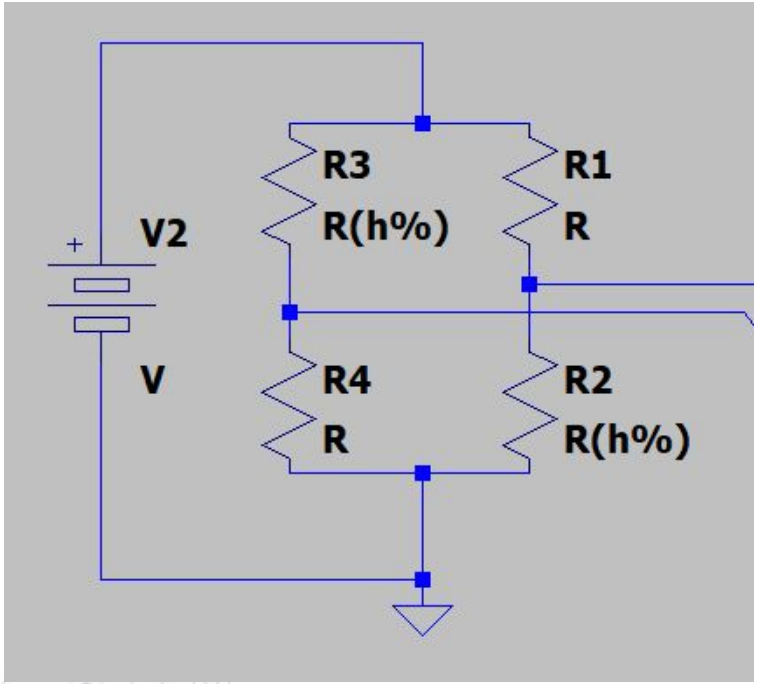


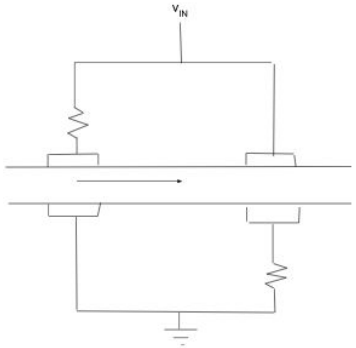
Figure 6: Graphs demonstrating the change in blood resistivity and conductivity relative to % hemolysis.[12]

Block Diagram of the System



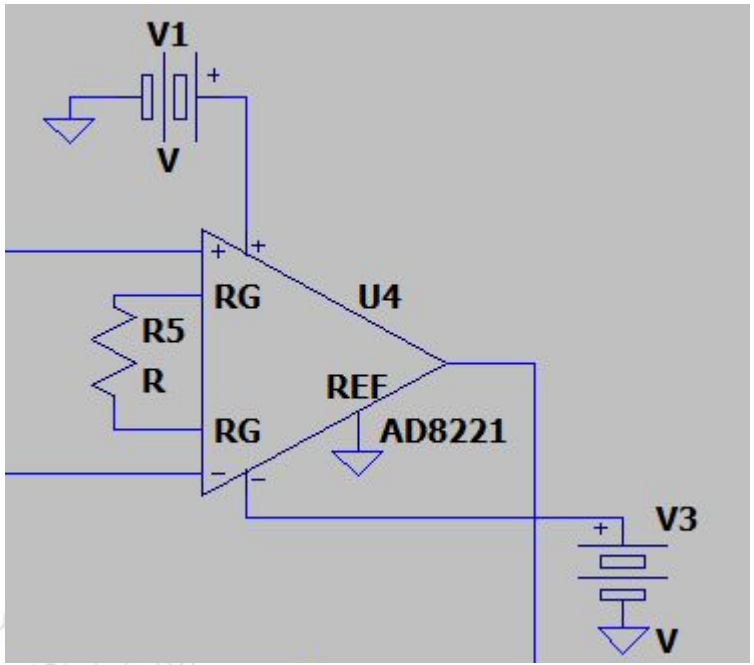
Device Parts: Wheatstone





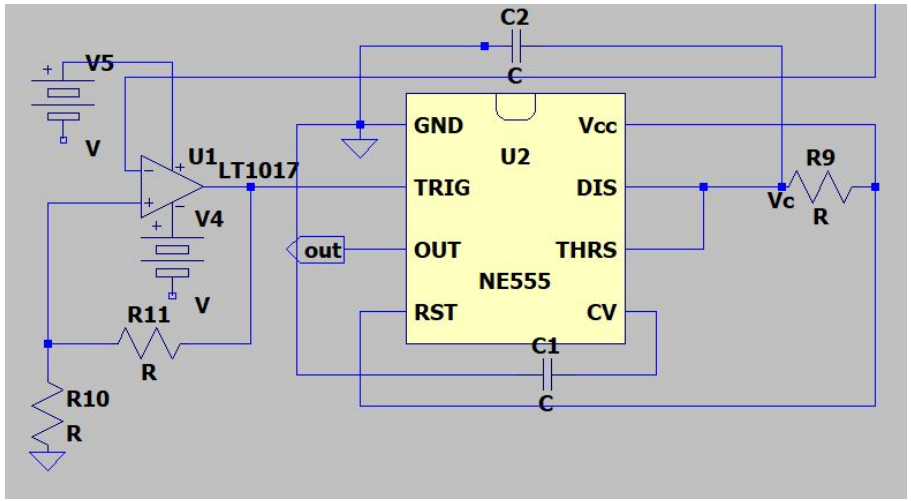
- Wheatstone bridge with two “strain gauges” - R is inversely proportional to %H
- 2 variable resistors provide better sensitivity
- 9V across the bridge

Device Parts: Instrumentation Amplifier



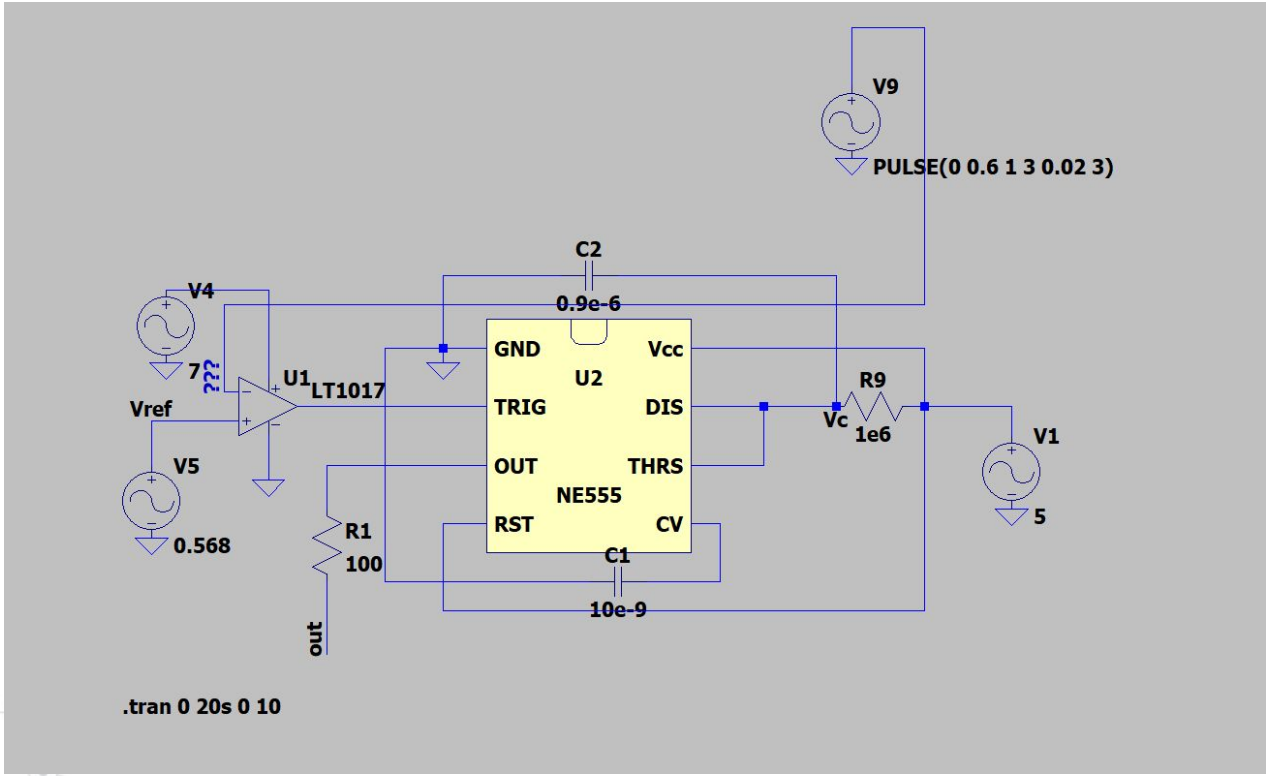
- Accurate amplification of WB output, regardless of resistor tolerances
- Less potential damage on circulation (high Z_{in})
- High CMRR (Potential noise due to machineries)

Device Parts: Comparator and 555

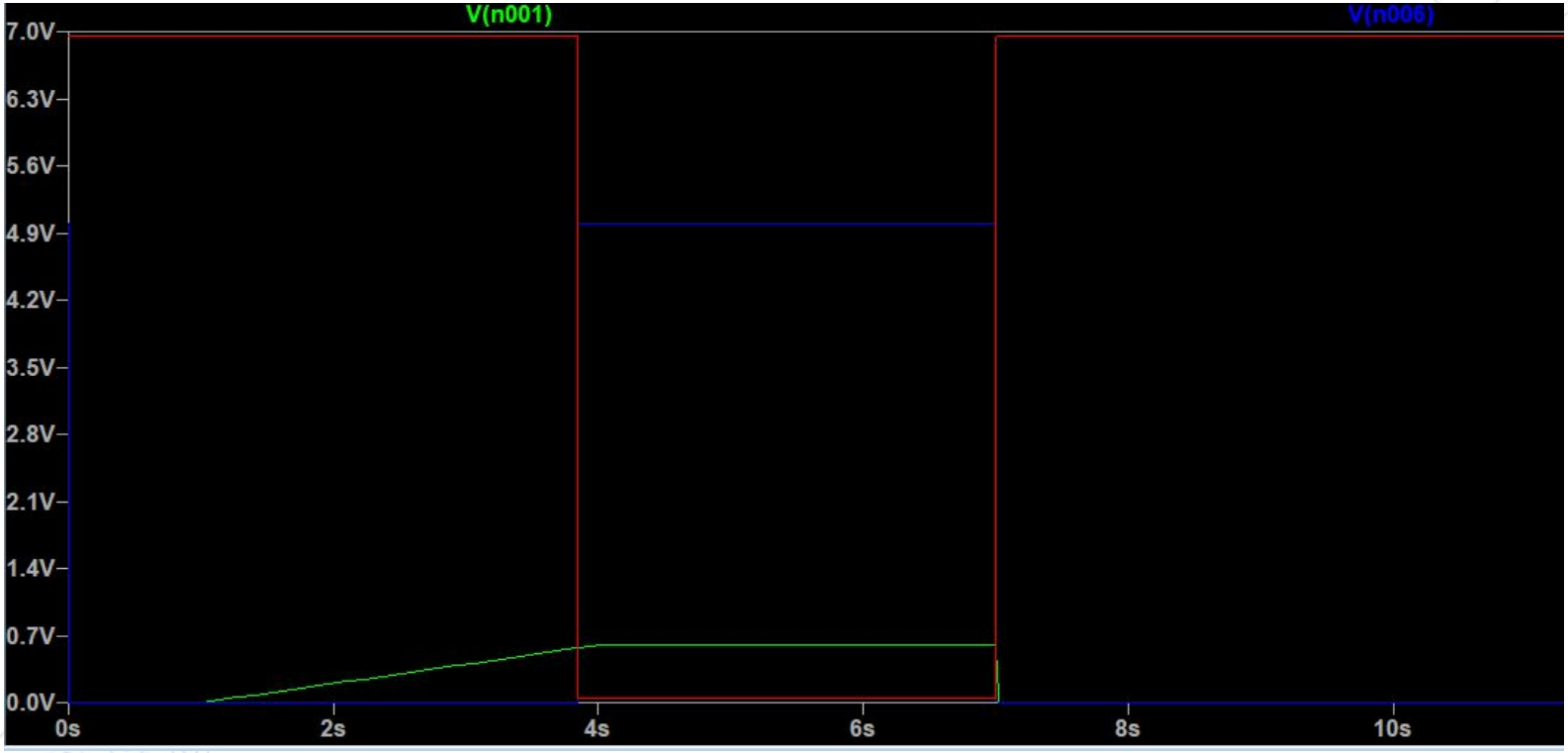


- Activation of pump when hemolysis level exceeds 2%
- 555 timer set to switch pump on for 1 second at a time
- Trigger cannot activate until hemolysis < 2%

Simulated Circuit with Values



Simulated Circuit Output



Conclusions

Hopefully with this design, we can reduce the stress on the body caused by hemolysis and its negative physiological effects.

This technique could be useful in medical procedures where mechanical shear results in the breakdown of the erythrocyte membrane.

Future Plans/ Improvements

- A sensor module that measures the concentration of free scavenging molecules
- Designing our own pump to dispense scavenging molecules
- Research conductivity changes due to free scavenging molecules
- Look into other pathologies that might affect blood conductivity

Weaknesses

- This design is blind to the differing concentrations of free hemoglobin, heme, and iron ions
  - Cannot tell how much of the change in conductivity is due to a particular molecule.
- Design is only designed to work with tracking hemolysis

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