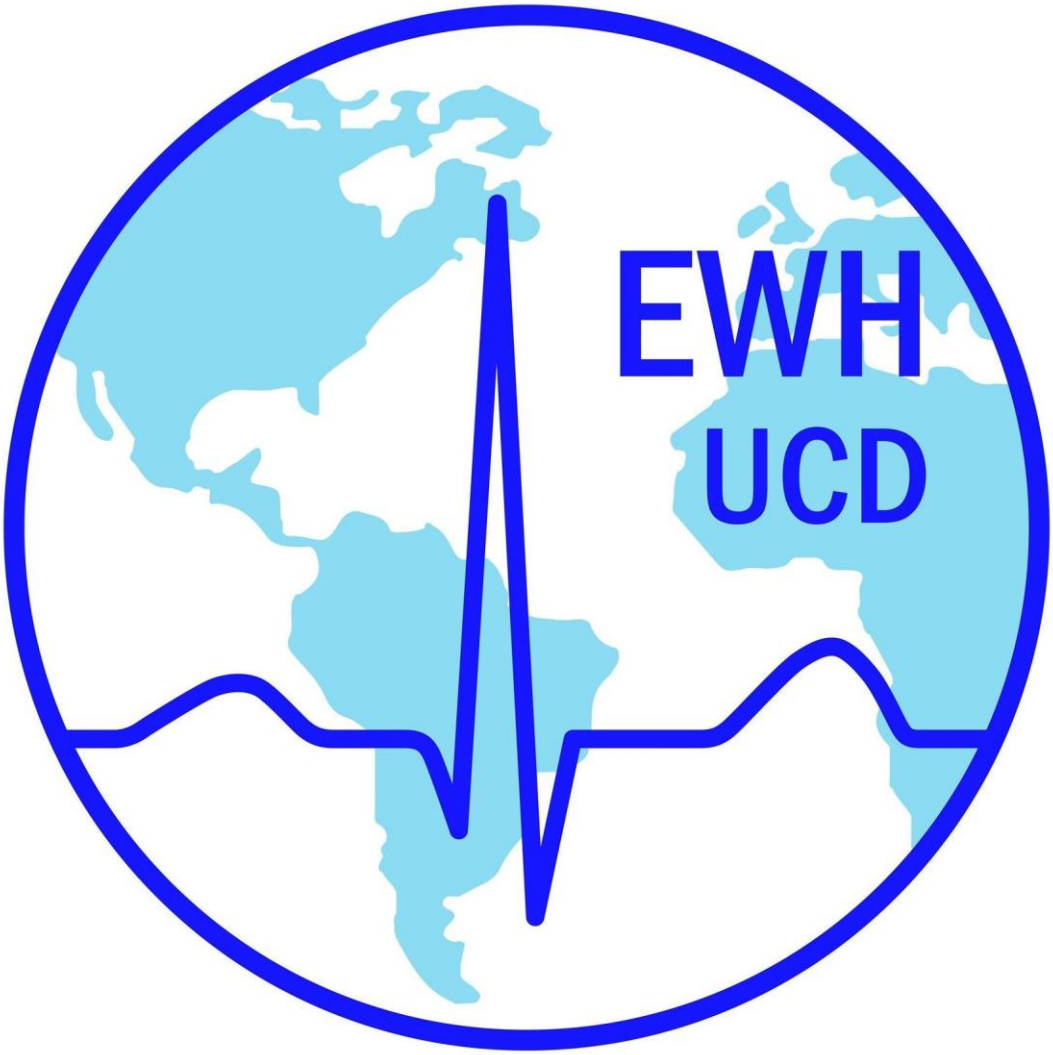


Engineering World Health Design Competition 2022

PneuDetect

An efficient point-of-use device for early detection and monitoring of pneumonia in infants in developing countries

Team members:

Sarthak Jain

Beryl Johnson

Nathan Hens

University College Dublin

Centre for Biomedical Engineering

EWH University College Dublin Chapter

Problem Definition

Pneumonia remains the primary infectious cause of death among children under the age of five, with devastating consequences. In 2019, pneumonia accounted for 14% of all child deaths globally [1]. With over 700,000 lives lost to pneumonia, equivalent to a child's death every 43 seconds, it remains a significant global health challenge [2]. Despite the availability of simple interventions and effective treatments that can prevent these deaths, pneumonia often goes unrecognized and untreated within communities until the child's condition becomes critical.

Current clinical methods for diagnosing pneumonia include X-ray imaging, biopsy procedures, and blood tests. These methods help healthcare professionals assess the presence of pneumonia in patients. Symptoms such as cough, fever, difficulty breathing, chest pain, and sputum production are also considered during diagnosis [3]. However, these methods have limitations in terms of specificity, invasiveness, and availability in resource-limited settings such as the inability of X-rays to detect specific pathogens and the time-consuming nature of biopsy procedures. Blood tests, although informative, can be invasive. Moreover, these methods can be time-consuming, making them unsuitable for routine clinical assessment. Therefore, there is a need for alternative approaches that offer non-invasive and efficient diagnostic options for pneumonia

In low and middle-income countries (LMIC) , pneumonia diagnosis relies on the World Health Organization's Integrated Management of Childhood Illness and Integrated Community Case Management (iCCM) guidelines, which primarily depend on subjective clinical signs and symptoms. Respiratory rate (RR) plays a crucial role in the accurate classification of pneumonia cases according to the iCCM criteria. However, a systematic review conducted by Rambaud-Althaus et al. revealed that relying solely on a single clinical sign, such as RR, is unlikely to enhance diagnostic precision for pediatric pneumonia [4]. This underscores the limitations of using subjective clinical signs as the sole basis for diagnosis.

The diagnostic yield of fast breathing as an indicator of bacterial pneumonia is low, suggesting that fast breathing may not be sufficiently sensitive or specific in diagnosing bacterial pneumonia [5]. These findings raise doubts about the reliability of RR as a diagnostic marker for pneumonia.

Current diagnostic methods for pneumonia in infants are not suitable for resource-limited settings. There is a need for an easily deployable device that can be used by healthcare workers in the infants' homes, providing quick and accurate diagnosis. This results in the clinical need statement that our solution is designed to address:

" To develop a low-cost, non-invasive, point-of-use device for early detection and monitoring of pneumonia in infants in developing countries and LMIC"

By addressing these challenges, our goal is to offer a reliable and cost-effective solution that improves the accuracy and efficiency of pneumonia diagnosis in infants. This will lead to better healthcare outcomes and alleviate the burden on healthcare systems in developing countries.

Our device utilizes an exhaled breath condensate (EBC) analysis module and an electrochemical sensor to overcome the limitations of existing methods. This enables early and precise screening, facilitating timely interventions and appropriate management of pneumonia cases.

Functionality and Technical requirements

The Pneudetect module consists mainly consists of two modules. The EBC module and the electrochemical sensor module.

The EBC module:

- Non-invasive diagnostic tests using exhaled breath condensates (EBC) are being developed as a rapid and comfortable method for diagnosing various respiratory diseases. EBC samples, which are collected and condensed using a temperature control device, have a composition similar to blood and lung fluid. They contain a range of compounds, including non-volatile molecules and water-soluble volatile compounds. EBC analysis shows promise as a diagnostic tool for inflammatory respiratory diseases [6].
- EBC is a complex low-protein matrix similar to blood and extracellular lung fluid, enriched with various compounds including non-volatile molecules, water-soluble volatile compounds, lipids, antibodies, and carbohydrates. It can contain up to 2000 different compounds [6,7].
- Through the use of a face mask, EBC may be effectively collected from newborn infants [10].

Electrochemical sensor:

For this project, CRP (C-reactive protein) and PCT (Procalcitonin) were investigated as potential biomarkers for non-invasive pneumonia diagnosis in exhaled breath condensates (EBCs). Previous research suggests that serum CRP can indicate ventilator-associated pneumonia (VAP) after antibiotic treatment, and serum PCT can predict short-term mortality in community-acquired pneumonia (CAP) [4].

Our device incorporates a two-valve system that ensures the flow of air during inhalation and directs exhaled breath into the collection tube. A Peltier module maintains the tube temperature at a constant 4 degrees Celsius. Patients breathe normally through the system for 10 minutes, allowing the condensate sample to accumulate along the tube. To collect the condensate, a plunger is manually used to push the sealed valve, acting like a syringe, and transfer the sample to the sensor. The sensor is specifically designed to detect CRP and PCT molecules, and a potentiostat is employed for functional activation. The results are displayed on an LED screen in a straightforward manner, indicating a positive or negative outcome. The device is user-friendly, requiring minimal operational knowledge for effective utilization.

Prototype designing and testing

- The initial model was designed in CAD with Fusion 360 and is shown in Figure 1

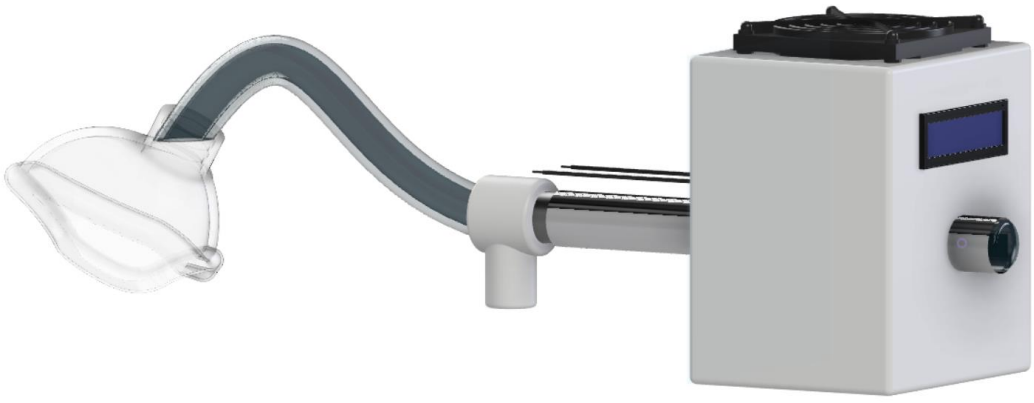
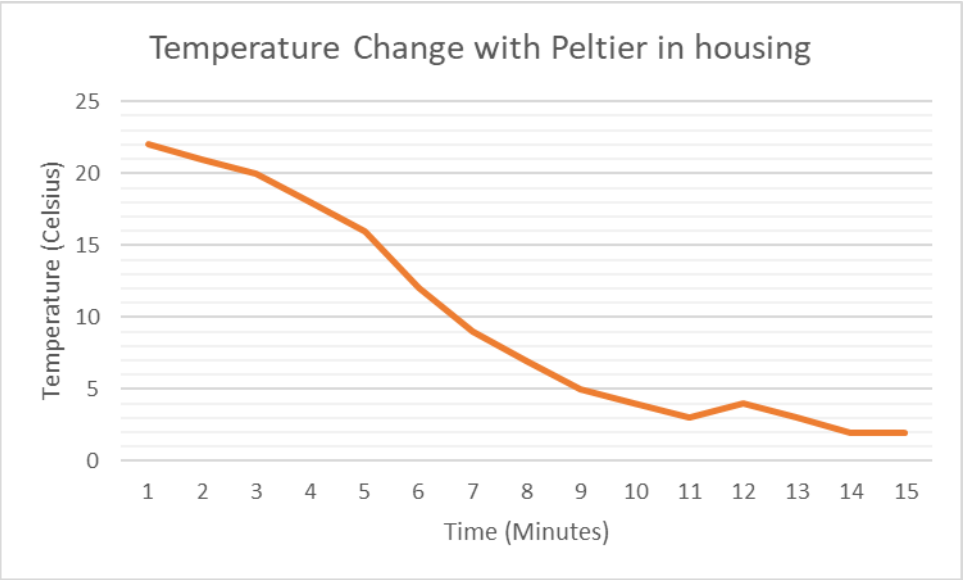


Figure 1: CAD model for PneuDetect

- The housing of the device, specifically the area where the Peltier module and the tube is located, is made of an insulated material.
- The test method for the Peltier module involved connecting the device to a 12V battery and placing a thermometer inside the tube. Measurements were taken at regular intervals, typically every minute, until the desired temperature was reached inside the tube. This test allowed you to evaluate the performance and efficiency of the Peltier module in achieving and maintaining the desired temperature levels. Results are shown below:



- It is determined from this testing that it takes 10 minutes to completely cool the housing before the EBC collection procedure starts.

Figure 2: Electrochemical sensor used

- ItalSens Gold (Figure 2) is a three-electrode electrochemical cell designed for analytical applications and consists of a gold working electrode, a silver pseudo reference electrode, and a gold counter electrode. The electrodes are produced using screen-printing technology, which allows for precise deposition of the electrode materials.
- To test the circuit functionality, the Arduino circuit was tested using a water detection sensor that had similar connections to the electrochemical sensor. When the circuit was powered on and the water sensor was placed in water, the red LED remained on until the sensor contacted the water, at which point the green LED turned on to indicate the presence of water. This confirmed that the circuit

connections were correct, and that the Arduino can communicate effectively with the electrochemical sensor

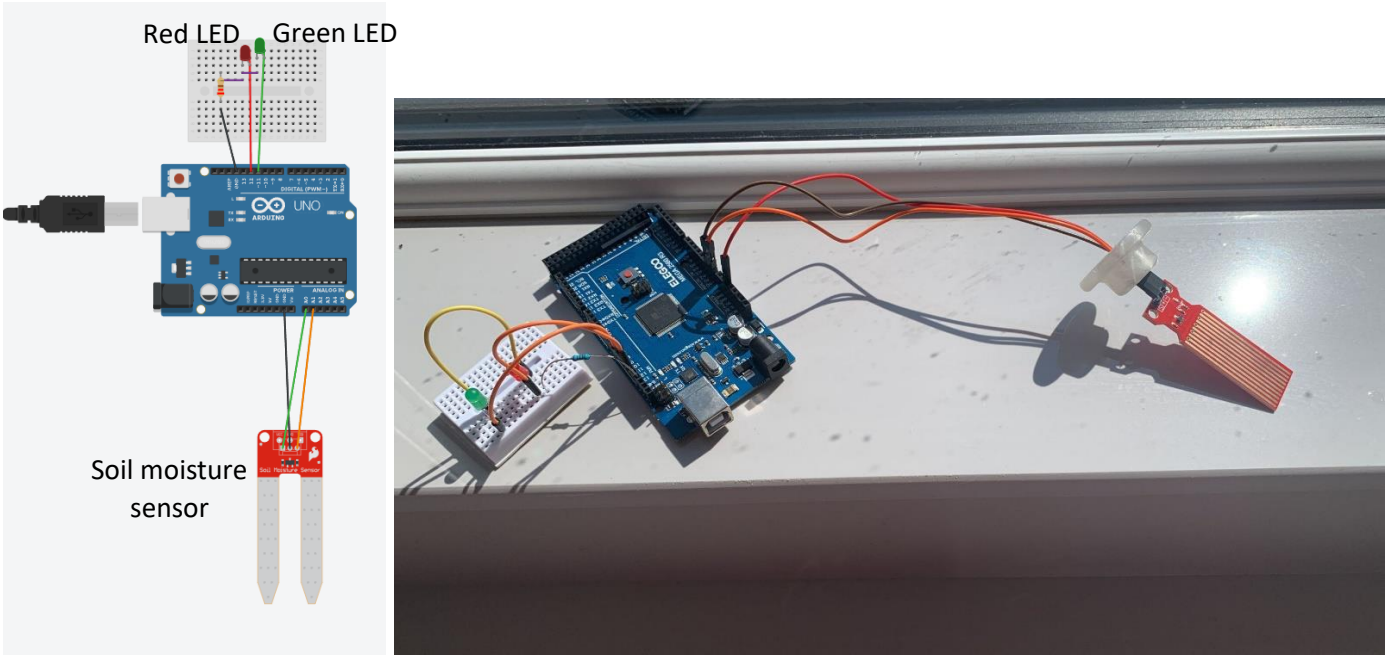


Figure 3: Circuit schematics and connection with the water sensor

Figure 4: Sensor with Plunger

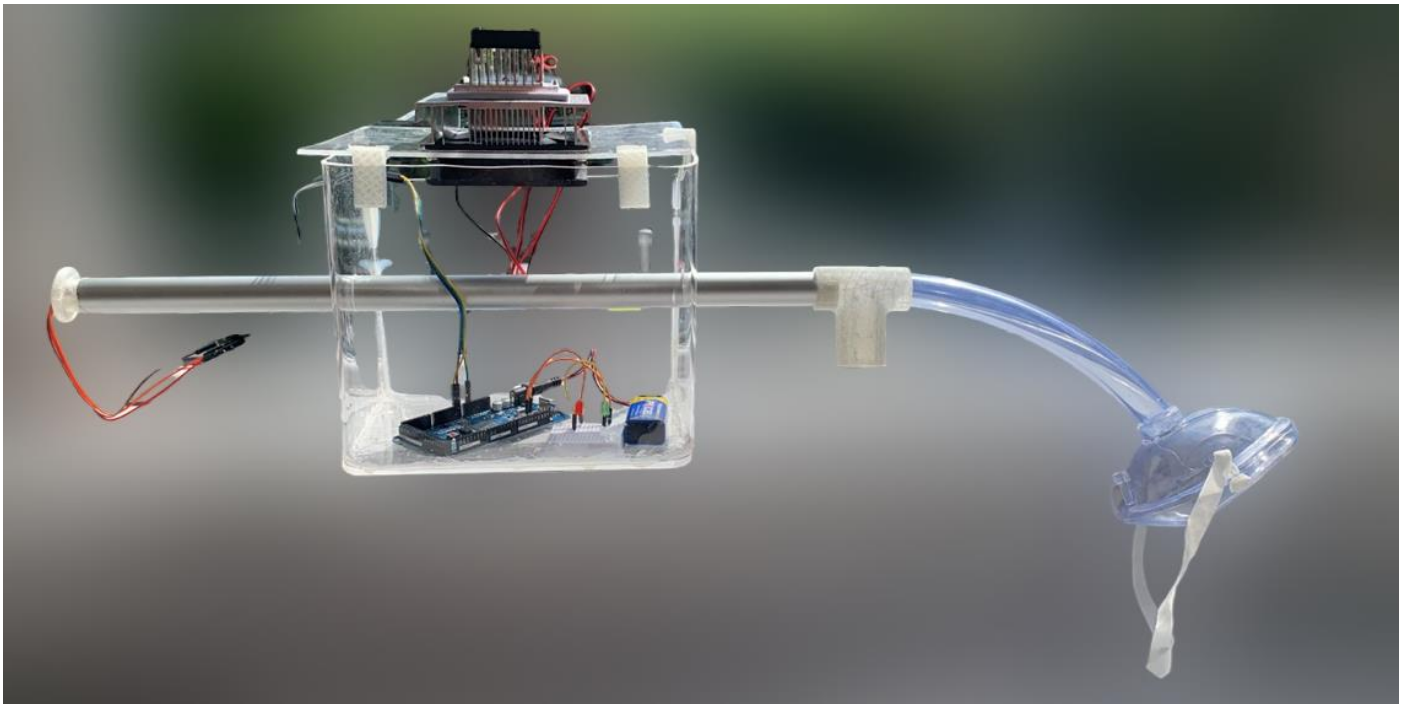


Figure 5: Final Prototype

- To test for the sensor a surface modification was performed. The screen-printed electrode was incubated for 24 hours in a polyelectrolyte solution. It was then washed with distilled water. To detect a protein an antibody protein with a buffer solution can be prepared and the sensor is incubated for 2 hours to functionalize it to work as a base template for sensing the specific protein. For the purpose of testing available antibodies in the university electrochemistry lab, antibody IgA was preferred instead of antibody CRP. The potentiostat was calibrated to measure the sensitivity of the sensor to the lowest possible value in order to detect the minimum available IgA value at 0.6V. Once this threshold was crossed the sensor gave a red light instead of a green light.

Impact on Global healthcare

Scaling up pneumonia treatment and preventive programmes might save the lives of 3.2 million children under the age of five, according to a Johns Hopkins University study. Pneumonia interventions alone have the potential to prevent nearly 9 million predicted under-five child deaths from all causes combined by 2030 [9]. This highlights the immense impact that targeted measures against pneumonia can have in saving lives and improving overall child health outcomes. With pneumonia claiming the lives of 800,000 children annually, the device has the potential to avert nearly 9 million child deaths in this decade. When combined with comprehensive interventions such as child nutrition enhancements, vaccination programs, new-born case management, improved water and sanitation, and appropriate antibiotic use, the device can save 3.2 million children from pneumonia and an additional 5.7 million children from other diseases between 2020 and 2030. These numbers demonstrate the significant progress that can be achieved through early detection and effective interventions. With a testing time of approximately 10-15 minutes, the device offers a quick and efficient method of diagnosis. Its portable nature allows healthcare workers to carry the device from house to house, eliminating the need for families with infants to travel to healthcare facilities and reducing stress and inconvenience. Healthcare workers can efficiently perform tests and provide timely interventions, improving healthcare outcomes.

Economic Feasibility and novelty

The R-Tube starter kit with a handheld plunger currently costs around 2000 €. However, our 3D printed device offers a significant cost reduction. Additionally, our device is portable and can be sanitized after each patient test, making it highly reusable compared to the R-Tube. By functionalizing the electrochemical sensor, we can expand the device's usability for diagnosing various diseases.

The exhaled breath condensate (EBC) contains a wide range of volatile organic biomarkers that can be utilized to detect different diseases. Exhaled breath condensate (EBC) has been used to diagnose respiratory diseases such as asthma, COPD, and pneumonia. It has also been useful in occupational settings and assessing pulmonary inflammation. EBC biomarkers have shown potential for diagnosing lung cancer and other pulmonary pathologies [11]. The EBC collection component remains the same for all these diagnostic applications, making it a versatile tool.

Component	Pricing
Arduino Uno Rev3	€24
Portable and Chargeable Battery (12V, 5A)	€20
Peltier Module	€23
ItalSens Gold SPE IS-W1-2.C1.RS.50 Electrochemical sensor	€5
Aluminium tube	€10
Acrylic housing and holders	3D printed (~€5)
Infant Breathing Mask	€5
One way Duckbill Valves	€10
Total cost	**€102**

In terms of cost, the prototype is priced at around 100 euros for single-use. However, it offers the advantage of being a one-time investment, as only the sensor requires replacement for each patient testing, and the tube necessitates sterilization. This eliminates the need for recurring expenses on the device itself, making it more cost-effective in the long run. Mass manufacturing plays a vital role in significantly reducing the overall cost of the device. This, in turn, enables the final product to be offered at a lower price point, making it more accessible and affordable for healthcare providers and patients.

PneuDetect is a Class 2 medical device according to the FDA. Therefore, we require a 510(k) clearance from the FDA before legally marketing them. The device will be distributed and administered through partnerships with charities and Non-Government Organizations (NGOs) that have connections to local clinics in developing countries. These partnerships will facilitate the training of local healthcare workers on how to effectively use and maintain the device. The device will be marketed to international charities focused on medical care, leveraging their networks and resources for distribution.

In addition, the team behind the device is participating in the NovaUCD Design competition, which provides support and resources for UCD undergraduate and postgraduate students looking to develop and grow start-up companies. This participation will help establish the device as a start-up enterprise, with the assistance and guidance of NovaUCD. By leveraging partnerships with charities, NGOs, and participating in entrepreneurship programs like the NovaUCD competition, the aim is to establish a sustainable business

model and effectively bring the device to market, ensuring its accessibility and impact in addressing the global health challenge of pneumonia in infants.

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Appendix

Arduino code:

```
/ this programme is for an Arduino to recognise an elevated voltage based on increased current through the sensor (Thanks to Simon Peter for helping out)

// if the voltage exceeds the threshold (indicating elevated igA) a red light blinks, otherwise a green light blinks

// a igA of 10mg/L is considered indicative of pneumonia in children

// a corresponding threshold voltage will have to be experimentally determined, but is assumed to be 600mV for now

// initialising all variables

int redLED = 2; //output

int greenLED = 3; //output

int sensor = A3; //input

int threshold = 600; //threshold voltage (in mV)

int reading = 0; //empty variable for reading



// setup function to define flow of information for operation

// this includes communication between arduino and other devices, as well as input and output channels

void setup() {
  // establish communication between devices
  Serial.begin(9600);

  //define GPIO pins connected to LEDs as output pins
  pinMode(redLED, OUTPUT);
  pinMode(greenLED, OUTPUT);

  // initialise both LEDs in OFF
  digitalWrite(redLED, LOW);
  digitalWrite(greenLED, LOW);
}
```

```
// loop function defines operation when switched on
// the sensed voltage is compared to the threshold, and the corresponding light will blink
void loop() {
  // assign read value to corresponding variable
  reading = analogRead(sensor);

  if (reading > threshold) { // high igA -> voltage above threshold
    // make red LED blink
    digitalWrite(redLED, HIGH);
    delay(250);
    digitalWrite(redLED, LOW);
    delay(250);
  }
  else { // low igA -> voltage below threshold
    // make green LED blink
    digitalWrite(greenLED, HIGH);
    delay(250);
    digitalWrite(greenLED, LOW);
    delay(250);
  }
}
```