Glucose Monitoring for Diabetes

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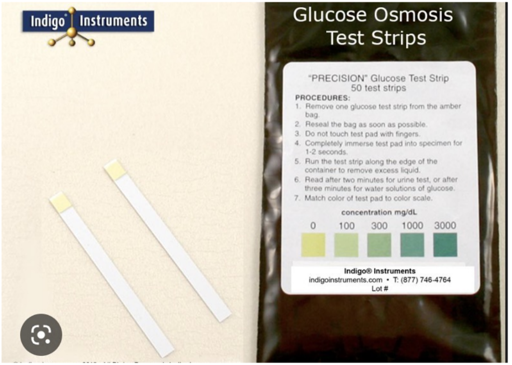
Motivation

1. Diabetes
    a. Diabetes is a group of disease that affect how the body store glucose in the blood.
        i. Eg: Insulin (regulates the intake of glucose in bloodstream in any moment).
    b. Defects in regulation blood sugar results in hyperglycemia or hypoglycemia
2. Glucose sensing
    a. Enzyme electrode-based test strip
    b. Color indicator (HRP) -based biosensors



Goal

1. Develop and simulate three electrodes glucose test strip
2. For the design of the test strip, interpretation of result should be easy

Design and Diagram

1. Sensor
   a. Reaction design and filters
   b. Three electrode test strip
   c. Op amp with 3 electrodes configuration
2. Circuit
   a. Full circuit design
3. Result
   a. Using ideal current source to simulate

Glucose Test Strip

- Voltammetry: 3 electrode
- Current from H_2O_2 oxidation is proportional to glucose concentration.
- The solution resistances and the double layer capacitors are very small can be ignored.

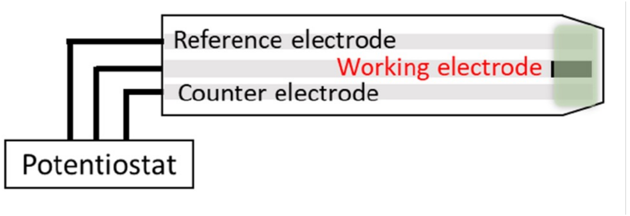


Figure 1. Schematic diagram of test strip[1].

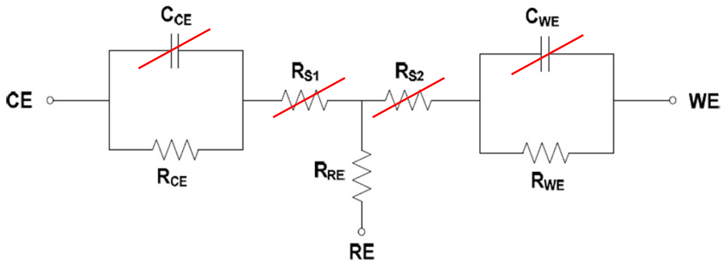
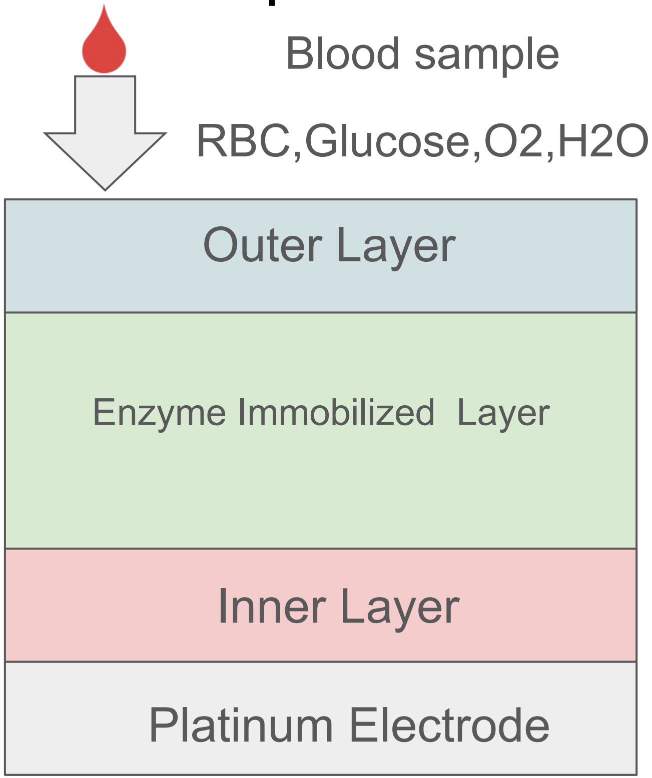


Figure 2. Equivalent circuit of an electrochemical cell[2].

Blown-up of the Working electrode



Outer Layer: filtering out RBC and catalase

Oxidation Layer: Immobilized with GOx.
glucose + O_2-*(GOx)*-> H_2O_2 + Gluconic Acid

Inner layer: Another filtering that only allow hydrogen peroxide to pass through.

Platinum Electrode: H_2O_2 is oxidized with a production of a current.

Look-Up Graph

- Voltammogram
- Did not conduct test with actual test strip
  ∴ use existing data
- Glucose level:

Glucose Level	Glucose Concentration	Current
Low	120 mg/dL	Below 12 μA
Normal	120-220 mg/dL	12 μA - 25 μA
High	220 mg/dL	Above 25 μA

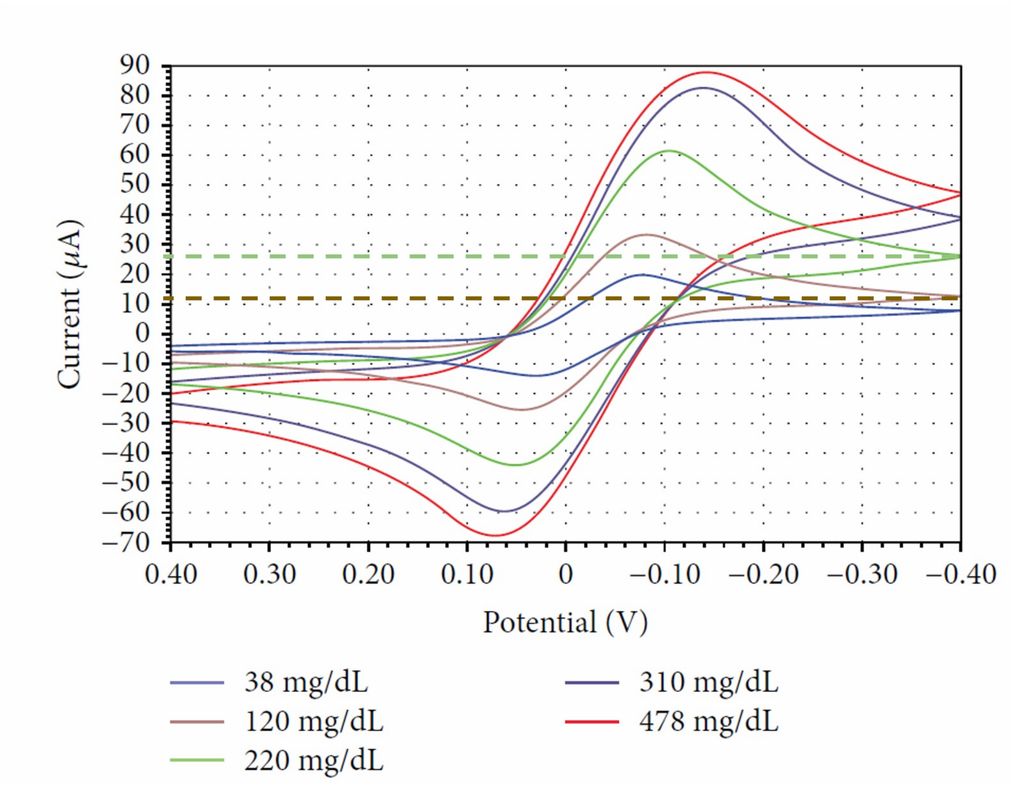
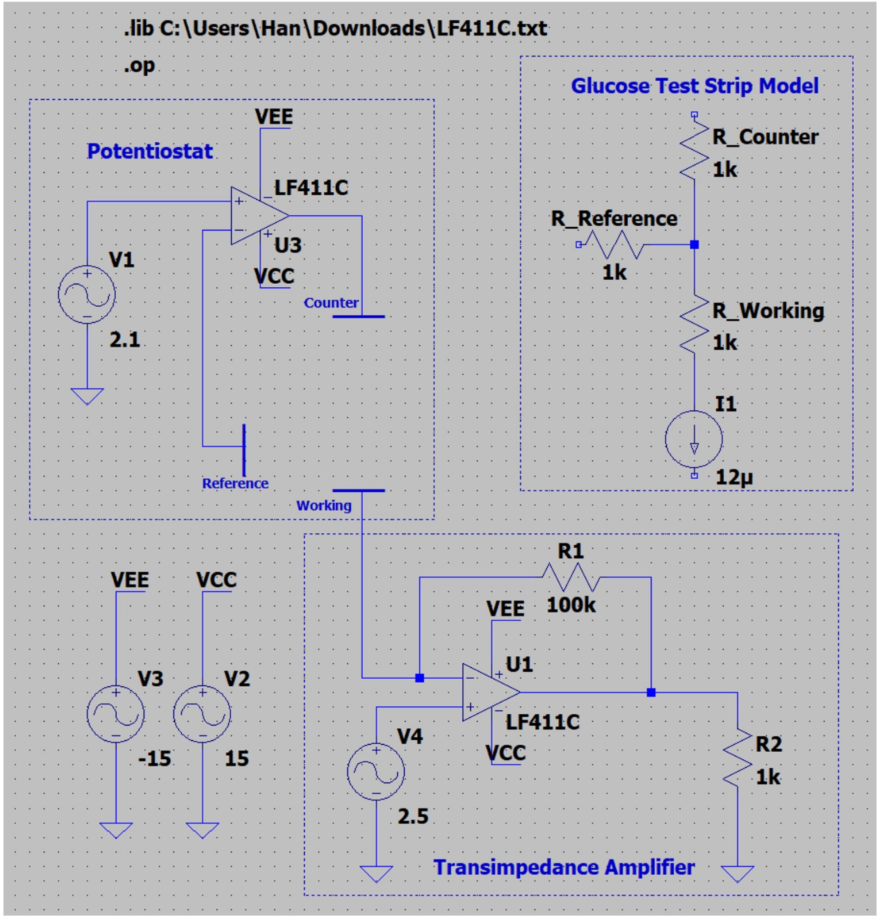


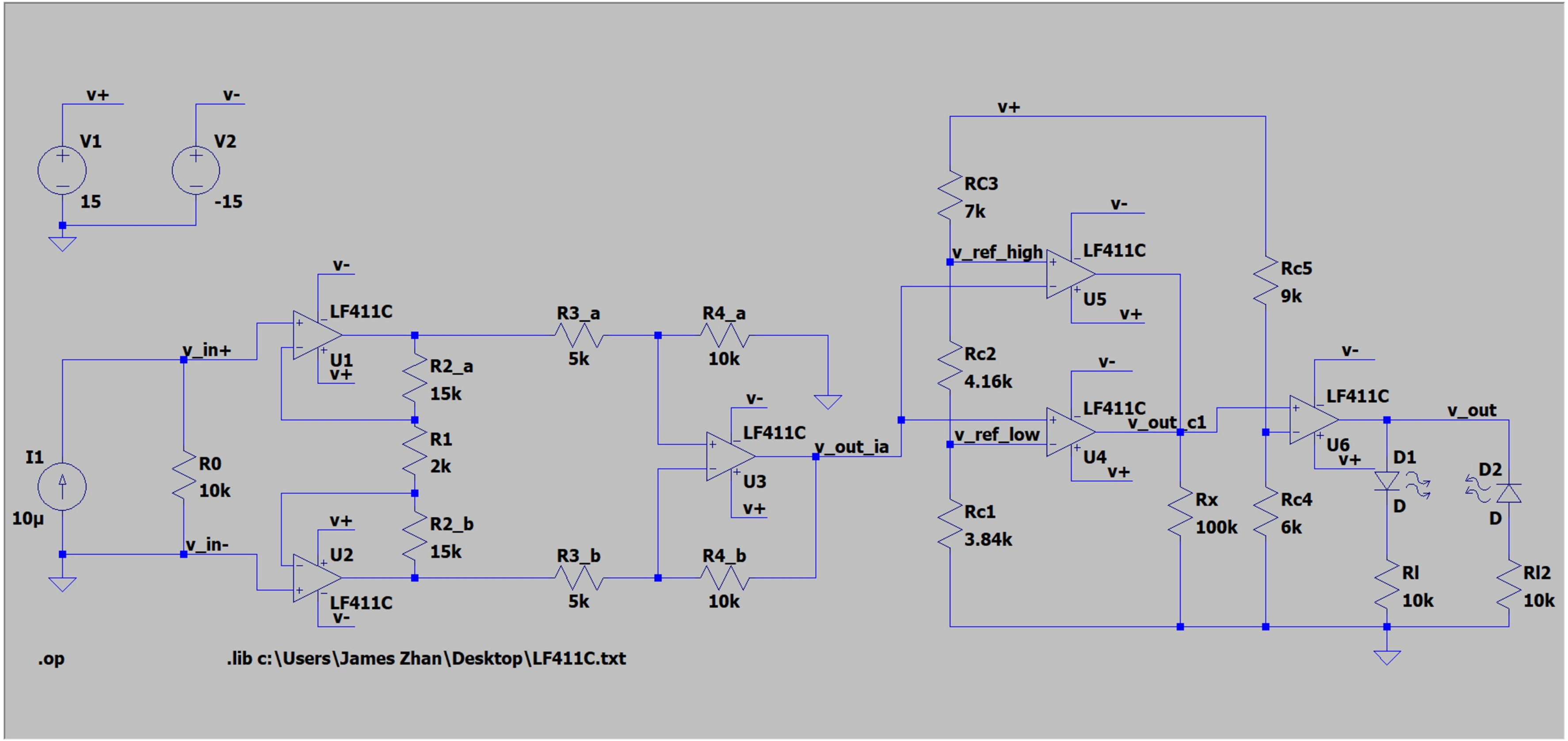
Figure 3. Electrochemical reaction current vs applied potential in the range of ±0.4V using standard solution of different concentrations[3].

Potentiostat Circuit

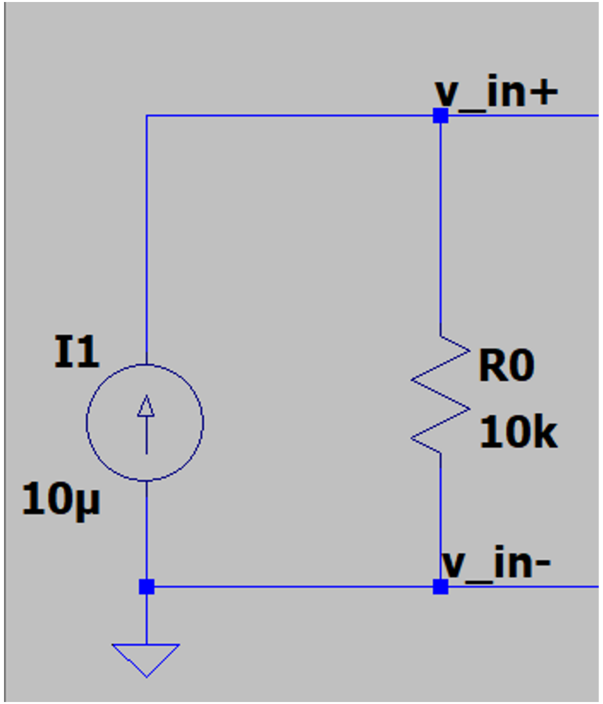
- 3 terminals: counter, reference, and working.
- Connect to a readout circuit
  - TIA
  - ADC
  - OTA
  - Current peak detector
- Low noise and low-leakage



Full circuit design

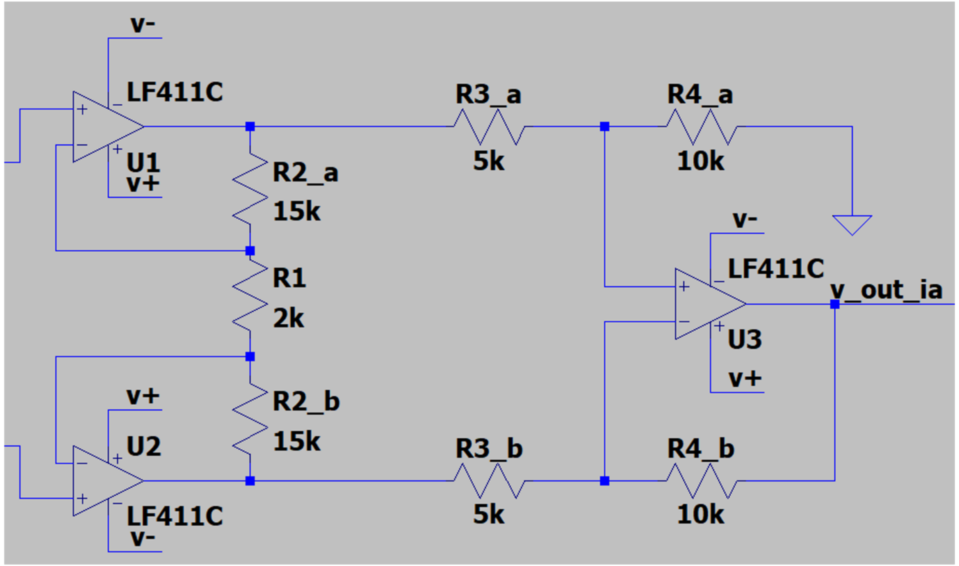


Full circuit design: I-V Converter



- The first part of the circuit is a current to voltage converter. Since we don't know what the actual measured current is, we assume the current is 10uA.
- Based on Ohm's law, this should give us a voltage output of 0.1V.
- We don't need to worry about resistance in parallel with R0 because R0 is connected to op-amp input. Op-amp input resistance is close to almost infinity.

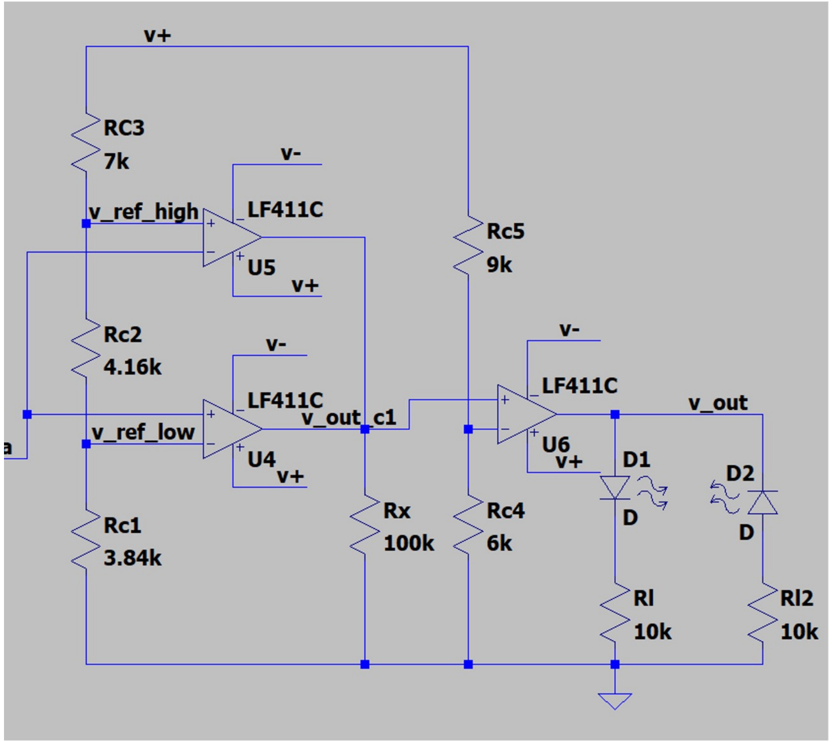
Full circuit design: Instrumentation Amplifier



$$A_d \approx -\left(1 + 2\frac{R_2}{R_1}\right) \cdot \frac{R_4}{R_3}$$

- We use an instrumentation amplifier to amplify the signal.
- Op-amp model we used are LF411C, powered by +15V and -15V.
- We don’t want the op-amp output to saturate, so we choose abs(Av) = 32v/v (first stage has gain 16v/v, second stage has gain 2v/v). This should give us v_out_ia =3.2v.
- V_out_ia is then passed to comparator.

Full circuit design: Comparators



- As given before, the normal upper limit for blood glucose level gives us measured current of **25uA**; normal lower limit for blood glucose level gives us measured current of **12uA**.
- To find the reference voltage for comparator, we passed current of 12uA/8uA through our design and got **V_ref_high = 8v** and **V_ref_low = 3.84v** (after amplification). Based on this, we choose Rc1, Rc2, and Rc3.
- For any current input **< 12uA**, v_out_c1 = 0v, v_out = v- = -15v, and **LED D2(red)** will be on.
- For any current input **> 12uA and < 25uA**, v_out_c1 = 15v, v_out = v+ = 15v, and **LED D1(green)** will be on.
- For any current input **> 25uA**, v_out_c1 = 0v, v_out = v- = -15v, and **LED D2(red)** will be on.
- Rl and Rl2 are placed to protect D1 and D2. Threshold voltage for LED is usually 0.7V. Big voltage across LED will break diodes.

Full circuit design: simulation result1(DC op)

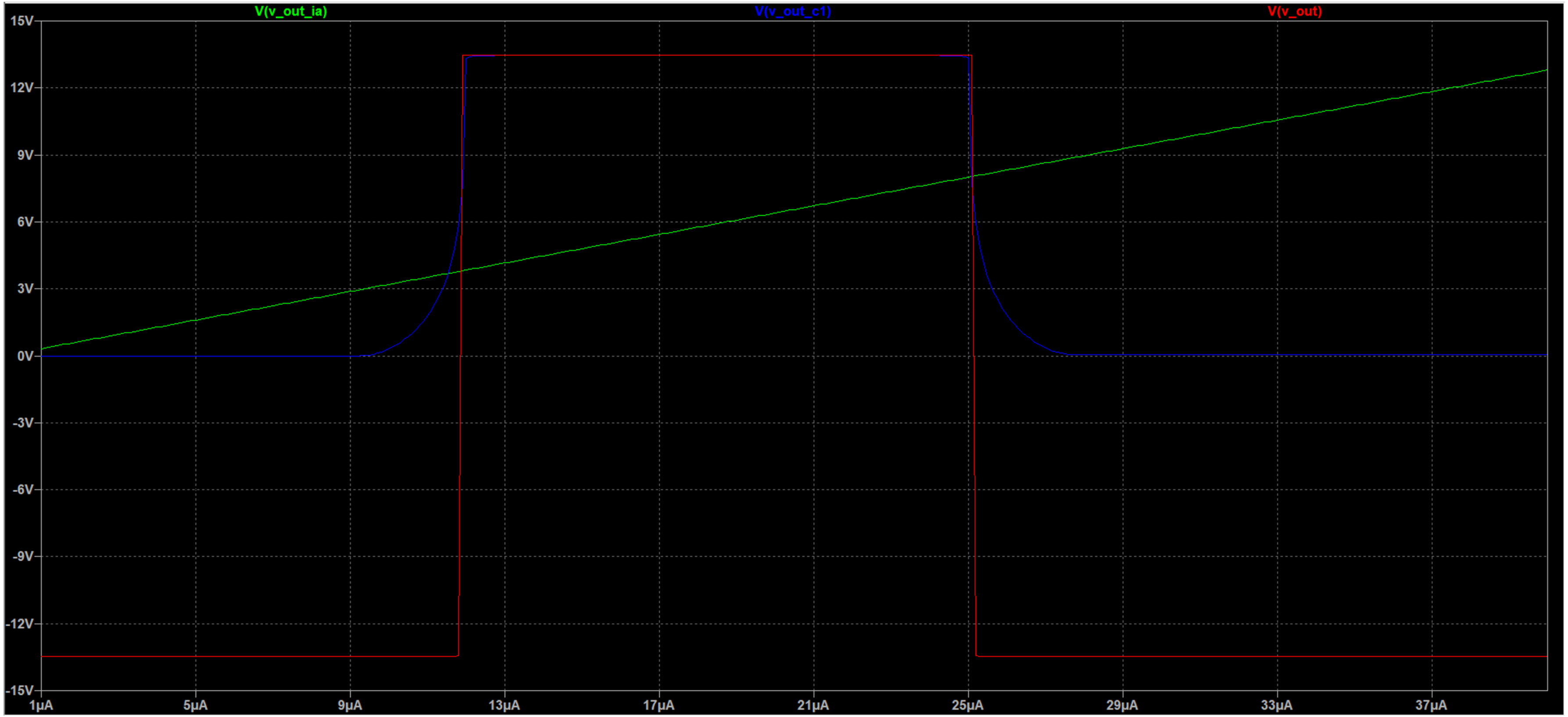
```
       --- Operating Point ---

V(v_in+):        0.0999996       voltage
V(n009):         -0.749932       voltage
V(v-):           -15             voltage
V(v+):           15              voltage
V(n006):         5.41313e-006    voltage
V(n001):         0.849935        voltage
V(n003):         0.0999971       voltage
V(v_out_ia):     3.19969         voltage
V(n005):         0.566608        voltage
V(n002):         0.566624        voltage
V(v_out_c1):     0.316135        voltage
V(v_ref_low):    3.84            voltage
V(v_out):        -13.4766        voltage
V(n007):         -1.34866e-007   voltage
V(v_ref_high):   8               voltage
V(n008):         -12.8151        voltage
V(n004):         6               voltage
I(D2):           0.00128151      device_current
I(D1):           -1.34866e-011   device_current
I(I1):           1e-005          device_current
I(Rx):           3.16135e-006    device_current
I(Rc4):          0.001           device_current
I(Rc5):          0.001           device_current
I(Rc3):          0.001           device_current
I(Rl2):          -0.00128151     device_current
I(Rc1):          0.001           device_current
I(Rc2):          0.001           device_current
I(Rl1):          -1.34866e-011   device_current
```

The DC operating point results are expected.

Key values are almost equal to our hand analysis.

Full circuit design: simulation result2 (DC sweep)



Advantages

- Easy interpretation of indication of normal or high/low glucose level
  - Green: you should be good
  - Red: watch out, you should see the doctor
- Instrumentation amplifier:
  - low noise
  - high CMRR ratio

Limitations and Improvements

- A platinum electrodes is not ideal for point of care tests due to its high costs. Future improvement may include finding an alternative electrode (such as a platinum coated carbon-based electrode).
- Variations in sample conditions, such as pH, could influence both the reaction and the readings. Future improvements need to account for the variation, such as adding buffers to the solution.
- **No actual measured data** of current value with respect to the glucose concentration.
- LF411C is usually powered by 15v and -15v supply, leading to high power consumption. Future improvements may include finding more energy efficient while close to ideal op-amp models.
- The I-V converter we used is relatively simple, which is vulnerable to noise or other influences. This can be improved by using op-amp to build the converter and use extra capacitors to eliminate noise.
- No differentiation for high glucose level or low glucose level. Can apply more LED colors to indicate.

Source

[1]J. Liu et al., “An AgNP-deposited commercial electrochemistry test strip as a platform for urea detection”, Scientific Reports, 2020.

[2]J Lai et al., “Design a Portable Bio-Sensing System for Glucose Measurement”, IEEE, 2011.

[3]K. Kim et al., ‘The Influence of Blood Glucose Meter Resistance Variation on the Performance of a Biosensor with a Gold-Coated Circuit Board’, Hindawi, 2019.