Study of Non-Invasive Devices for Health Monitoring

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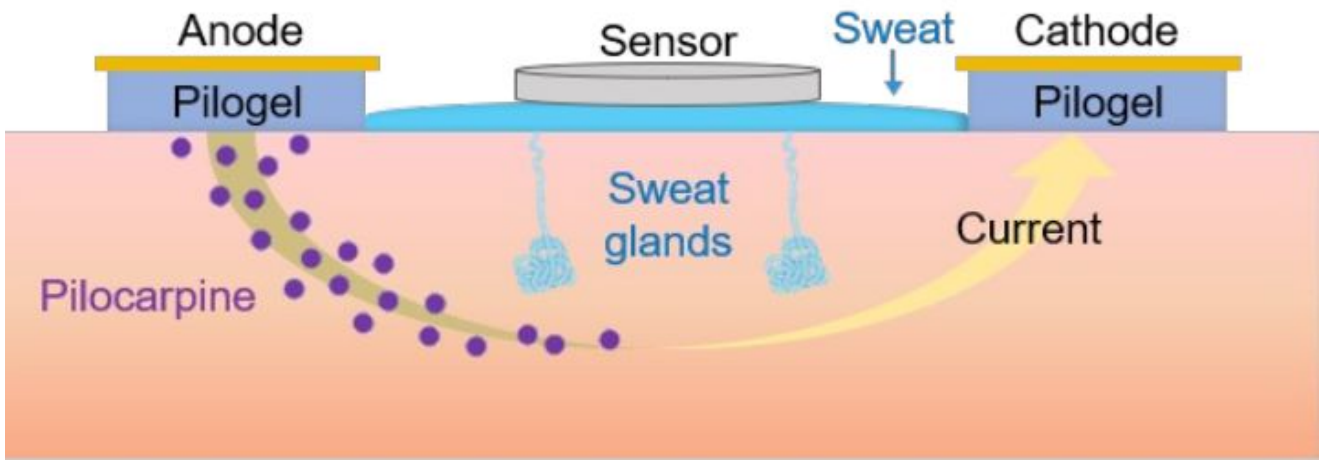
Sweat Detection and Analysis

- Several biomarkers available in sweat.
- Sweat secreted can be obtained can be easily obtained.

Target Analyte		Concentration in Sweat	Recognition Element	Sensing Modality
Ions	Na^+	10–100 mM	Na+	Potentiometry
	Cl^-	10–100 mM	Ag/AgCl	Potentiometry
	K^+	1–18.5 mM	K+	Potentiometry
	Ca^{2+}	0.41–12.4 mM	Ca2+	Potentiometry
	pH	3–8	Polyaniline	Potentiometry
	NH^{4+}	0.1–1 mM	NH4+	Potentiometry
	Zn^{2+}	100–1560 μg L^{-1}	Bi	Square wave stripping voltammetry
	Cd^{2+}	<100 μg L^{-1}	Bi	Square wave stripping voltammetry
	Pb^{2+}	<100 μg L^{-1}	Bi, Au	Square wave stripping voltammetry
	Cu^{2+}	100–1000 μg L^{-1}	Au	Square wave stripping voltammetry
	Hg^+	<100 μg L^{-1}	Au	Square wave stripping voltammetry
Drugs	Levodopa	<10 μM	Au	Chronoamperometry
	Caffeine	<40 μM	Carbon	Chronoamperometry
	Alcohol	2.5–22.5 mM	Carbon	Chronoamperometry
Metabolites	Glucose	10–200 μM	Glucose oxidase	Chronoamperometry
	Lactate	5–20 mM	Lactate oxidase	Chronoamperometry
	Uric acid	2–10 mM	Carbon	Cyclic voltammetry
	Cortisol	8–140 μg L^{-1}	ZnO, MoS2	Electrochemical impedance spectroscopy
	Ascorbic acid	10–50 μM	Carbon	Chronoamperometry
Biomolecules	Peptides	0.1 pM–0.1 μM	Au	Chronoamperometry
	Antimicrobial peptides	-	Carbon	Resistance

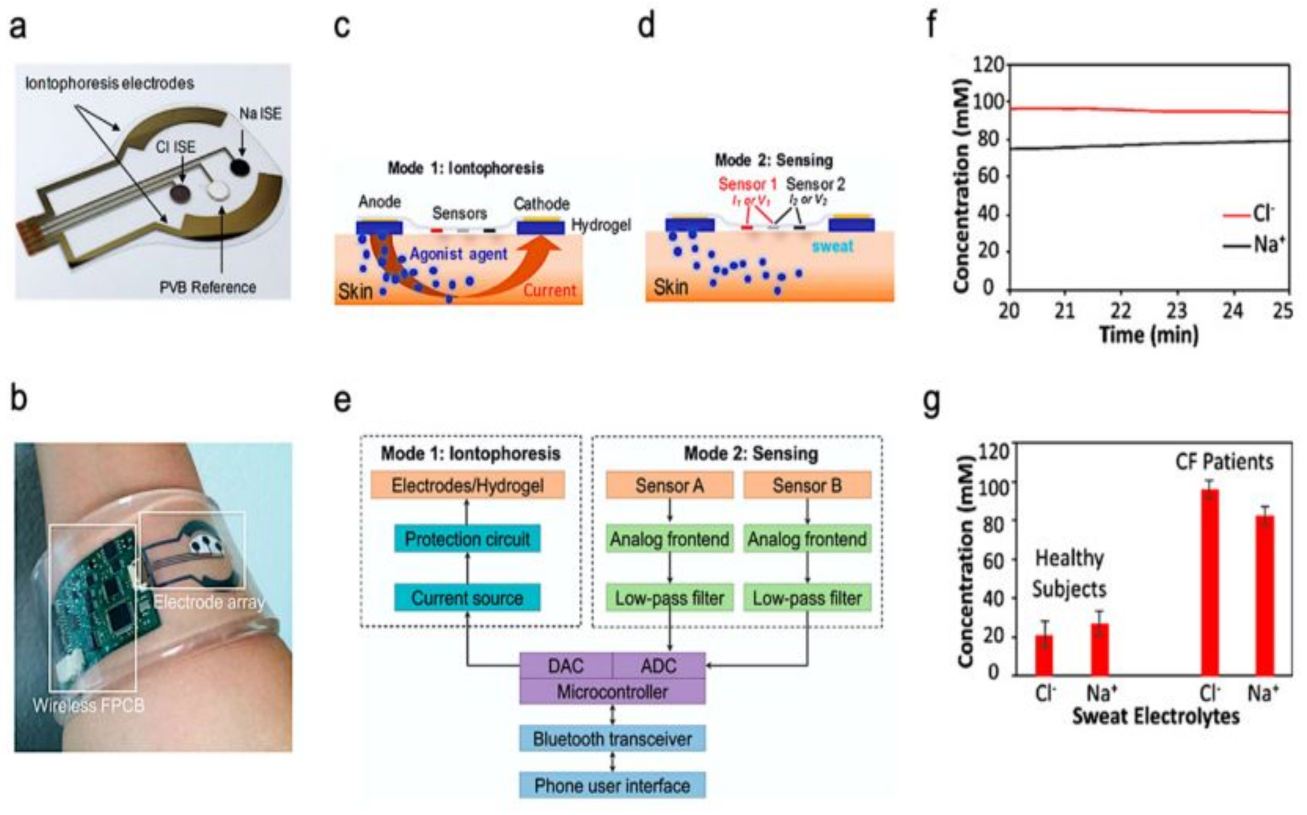
Sweat Extraction

- Iontophoresis is one of the commonly used sweat detection methods
- It depends on local sweat stimulation through the application of topical current



Applications

- Disease Detection and Monitoring
  - Cystic Fibrosis Diagnosis
    - Sweat chlorine concentrations has been a widely used metric for cystic fibrosis detection



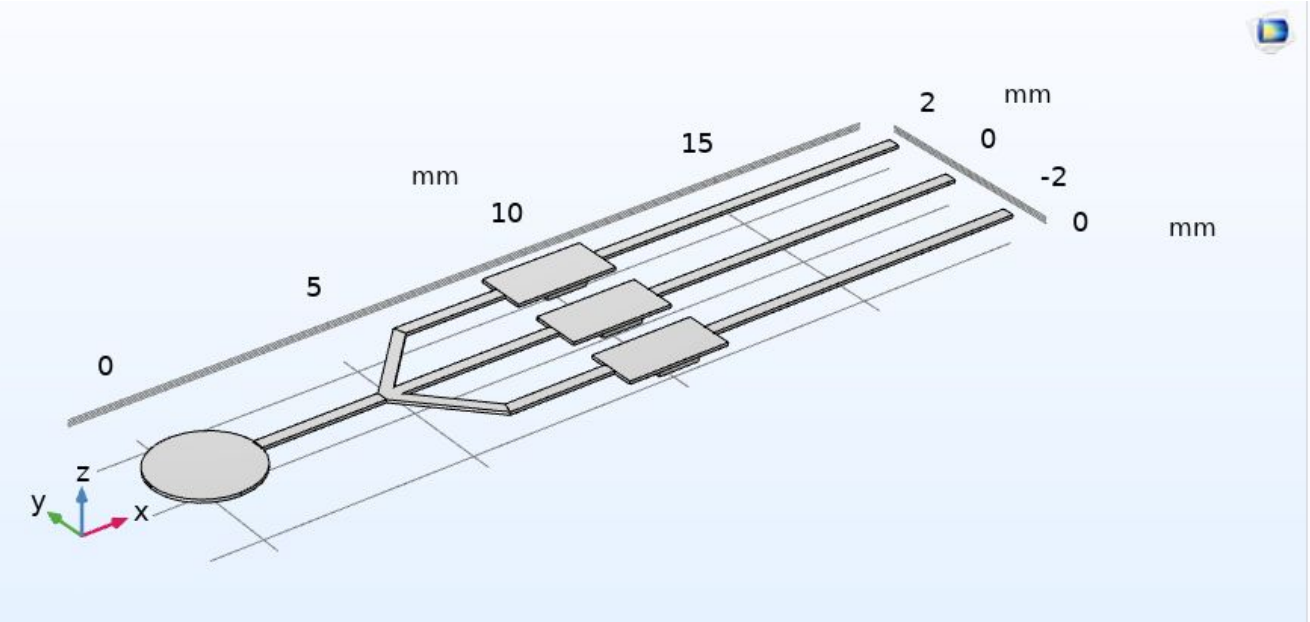
Applications

- Diabetes Monitoring
  - Sweat glucose levels has been shown to be directly related to diabetes.
  - While other methods do exist, sweat based detection allows for painless treatment of diabetes and reduces equipment size.

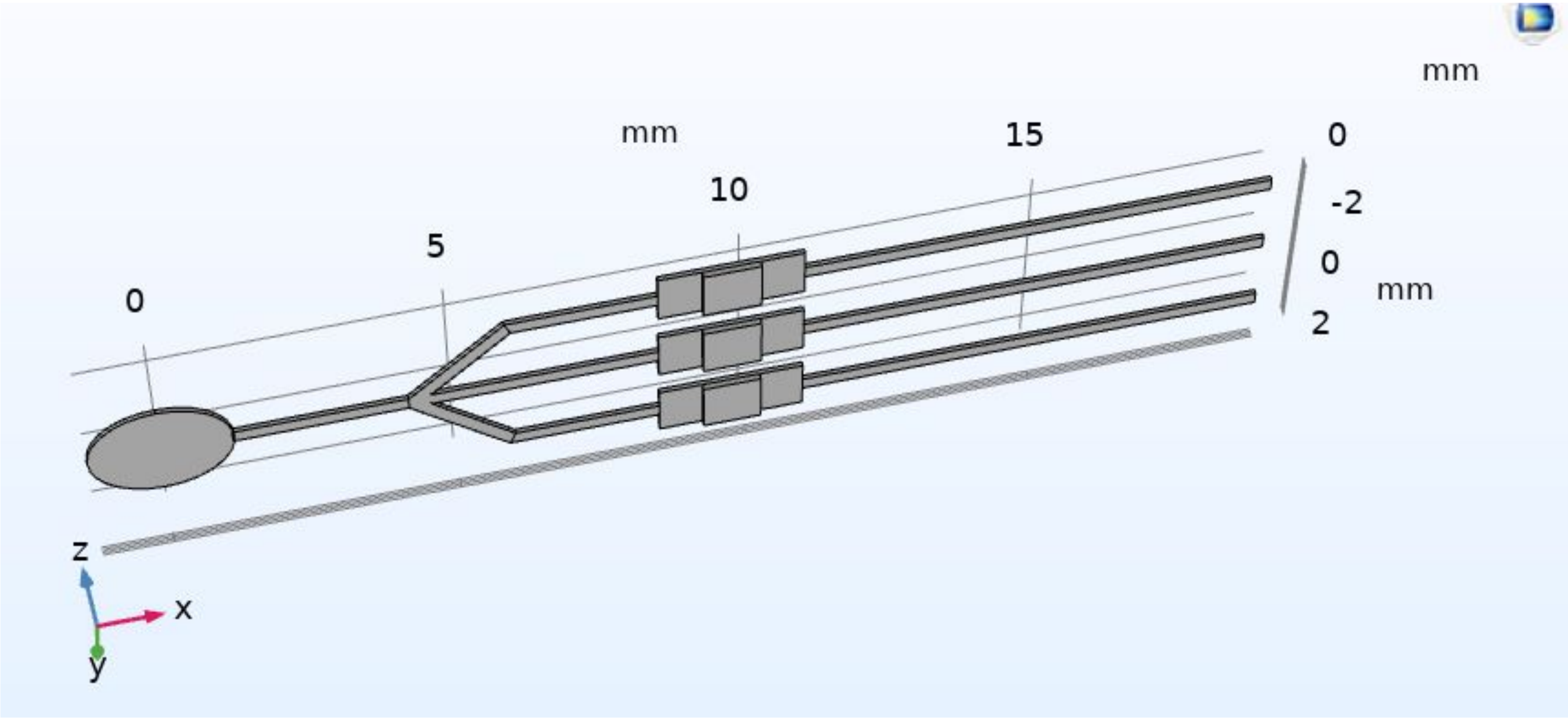
Microfluidic Electrochemical Detection System

Sensor

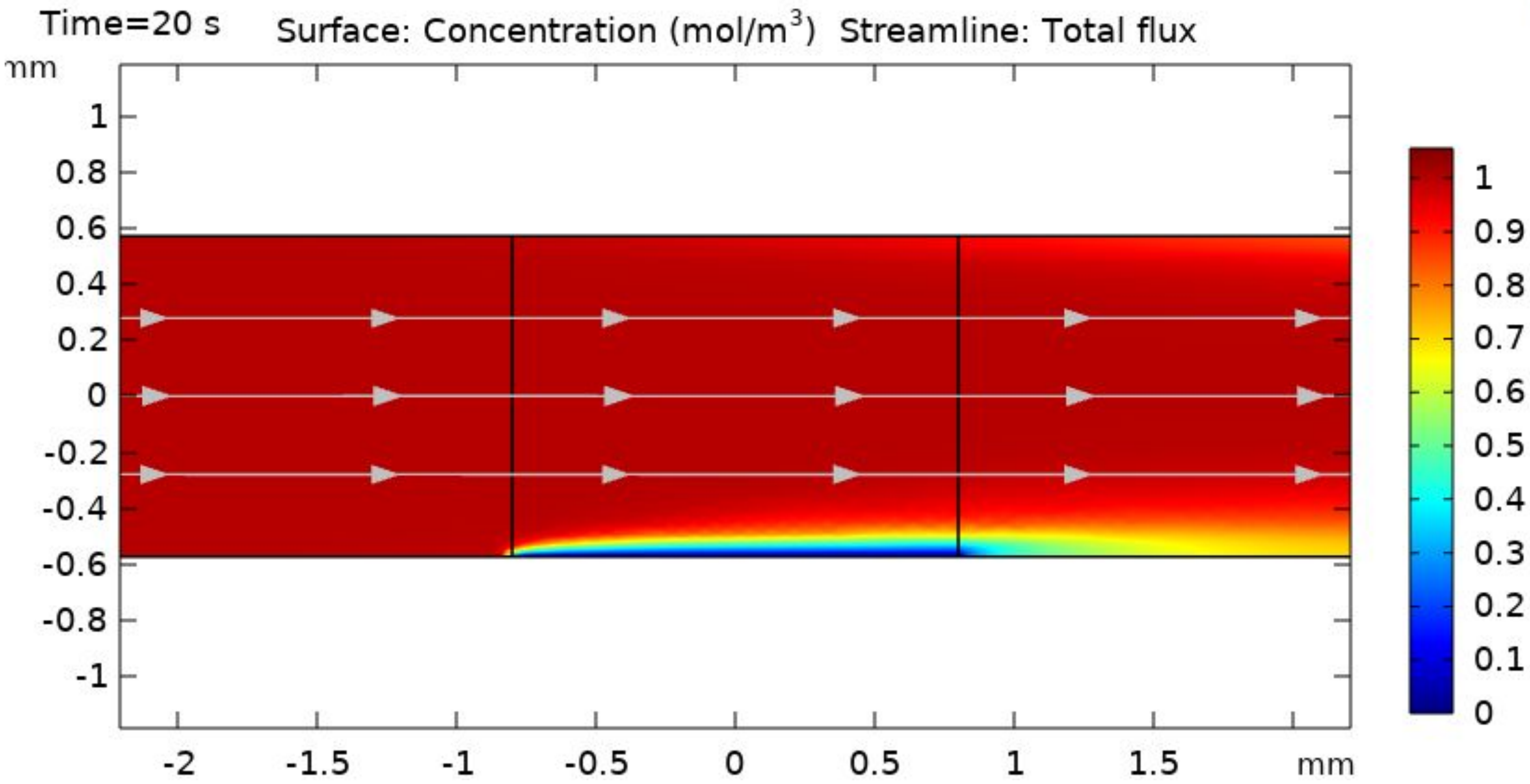
- Sensor detects and monitors 3 biomarkers – glucose, sodium and chlorine levels in sweat



Microfluidic Electrochemical Detection System



Microfluidic Electrochemical Detection System

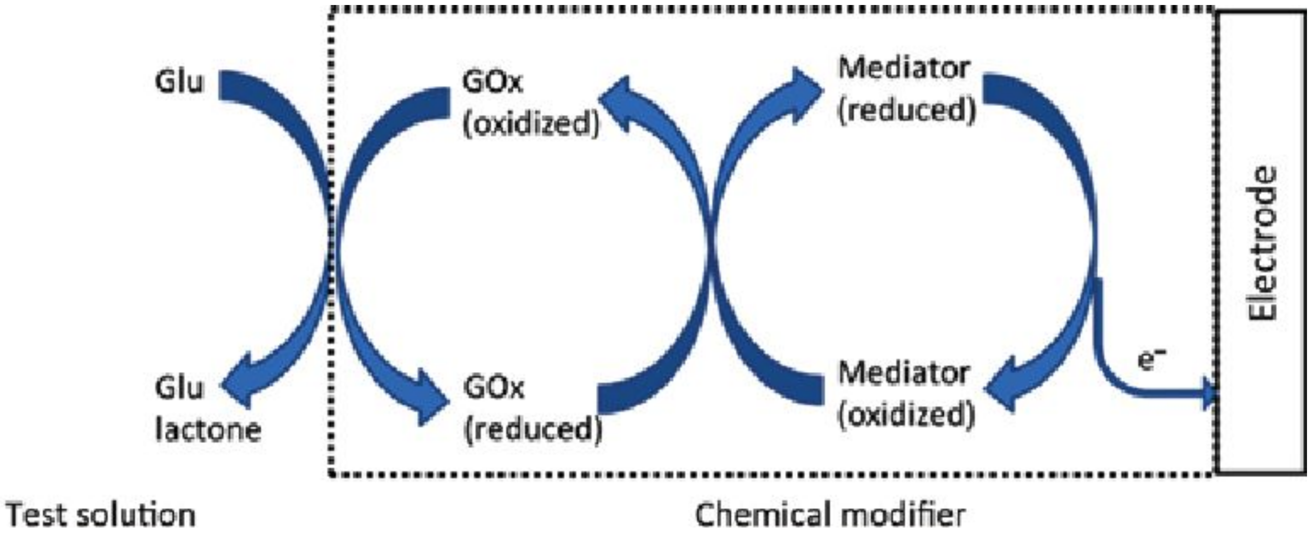


Microfluidic Electrochemical Detection System

- Electrochemical biosensors are normally based on enzymatic catalysis of a reaction that produces or consumes electrons (such enzymes are rightly called redox enzymes).
- The sensor substrate usually contains three electrodes; a reference electrode, a working electrode and a counter electrode.
- The target analyte is involved in the reaction that takes place on the active electrode surface, and the reaction may cause either electron transfer across the double layer (producing a current) or can contribute to the double layer potential (producing a voltage).
- We can either measure the current (rate of flow of electrons is now proportional to the analyte concentration) at a fixed potential or the potential can be measured at zero current (this gives a logarithmic response).

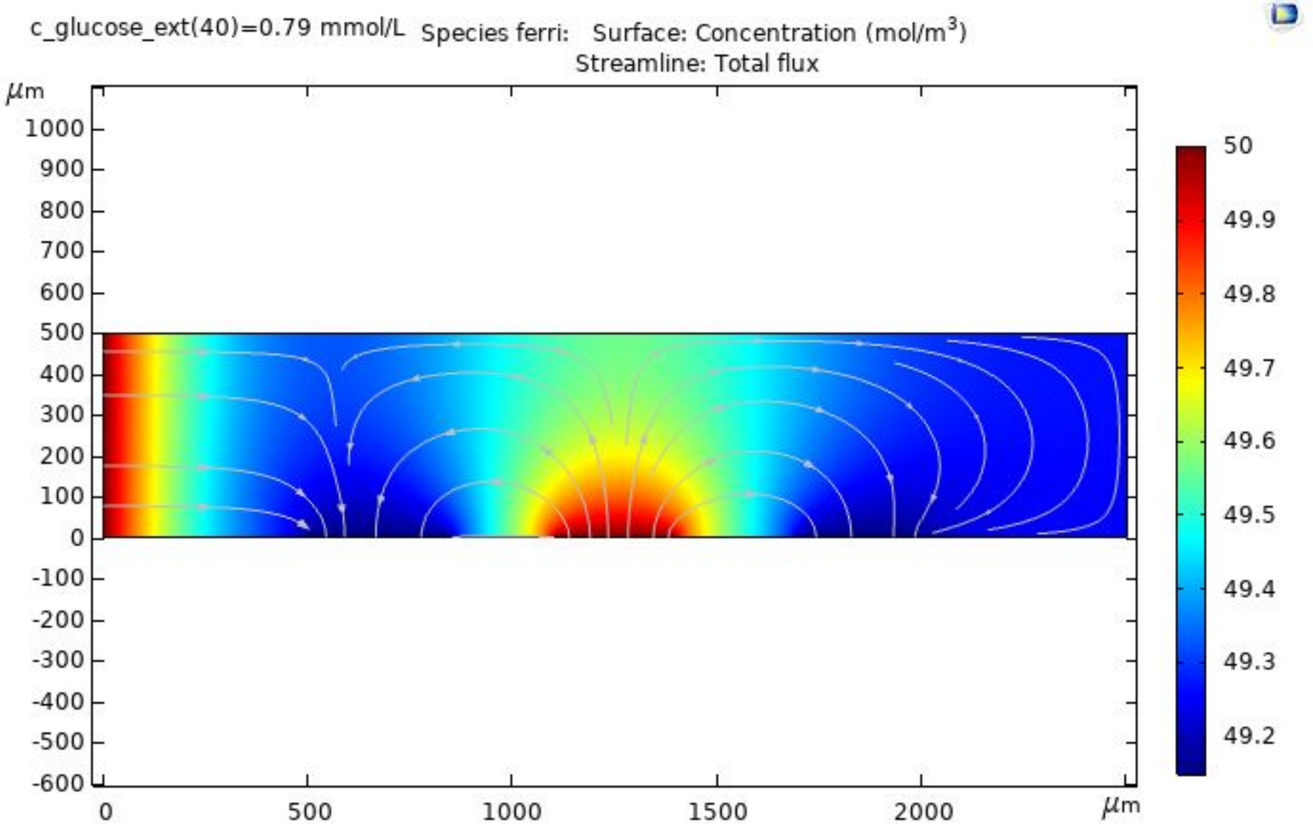
Microfluidic Electrochemical Detection System

- Glucose – Uses Amperometric Sensing
- Amperometry in chemistry is the detection of ions in a solution based on electric current or changes in electric current. Enzyme mediated electrochemical reaction.
- Simulation of glucose amperometric biosensor is being used from the COMSOL model. The oxidation of glucose is done by glucose oxidase, and further this is mediated by an inorganic oxidant with fast electrode kinetics, ferricyanide.



Microfluidic Electrochemical Detection System

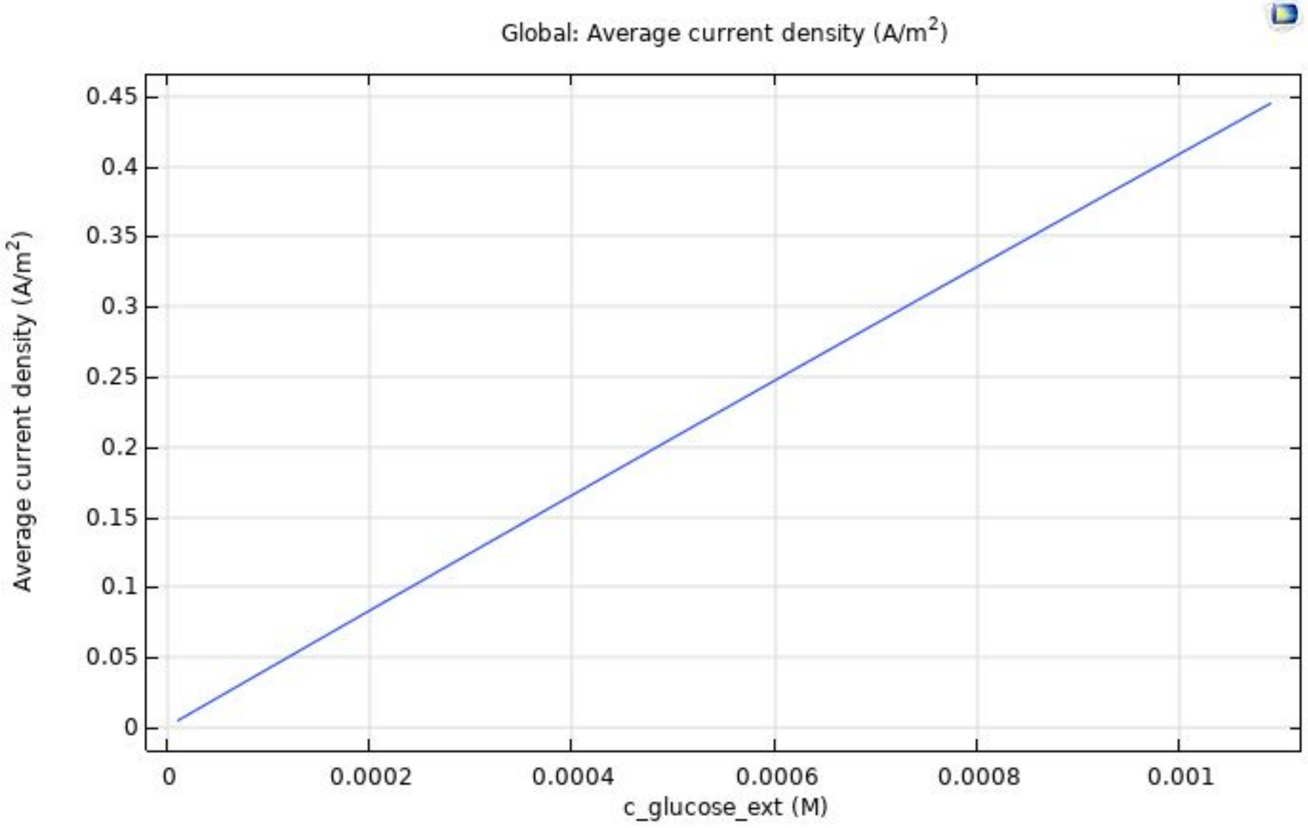
- Molar Concentration per unit volume over the sensor



Microfluidic Electrochemical Detection System

- Average Current Density versus Glucose Concentration
- Diffusion is modelled using Fick's law
- Current density is proportional to the flux and product species according to Faraday's laws of electrolysis

$$-\mathbf{n} \cdot \mathbf{J}_i = \frac{\nu_i i_{\mathrm{loc}}}{nF}$$



Microfluidic Electrochemical Detection System

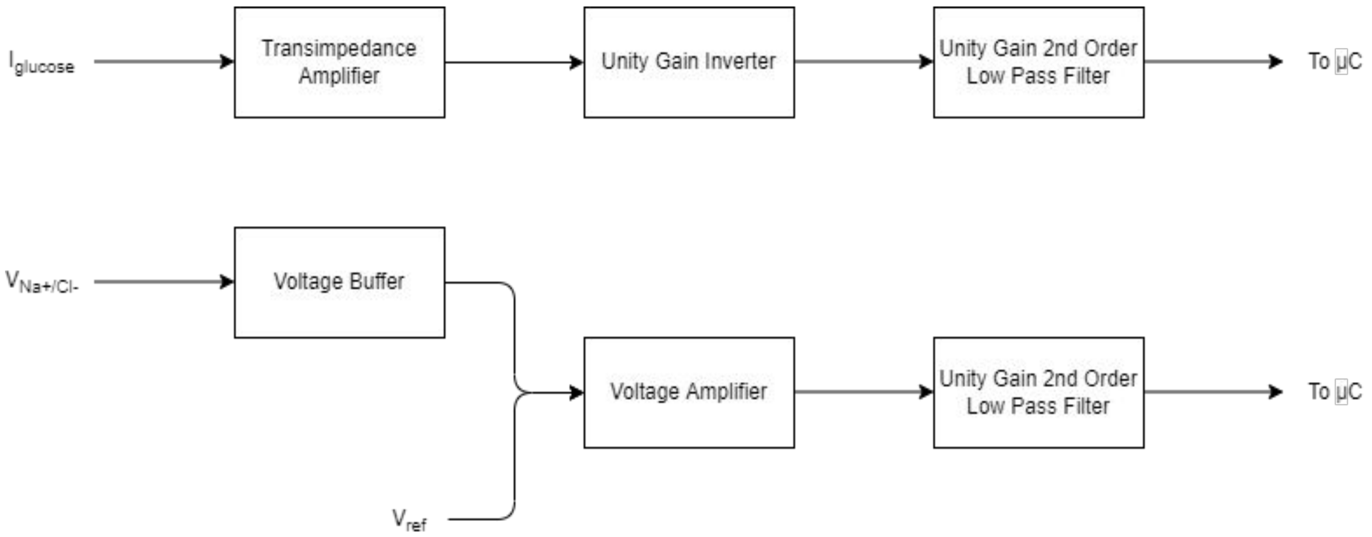
- Na^+, Cl^- - Ion Selective Electrodes
- An ideal I.S.E. consists of a thin membrane across which only the intended ion can be transported. The transport of ions from a high conc. to a low one through a selective binding with some sites within the membrane creates a potential difference.
- The voltage is theoretically dependent on the logarithm of the ionic activity, according to the Nernst equation.
- The normal range of electrolyte values in sweat in adults is up to 70 mmol/l (Na^+) and 55 mmol/l (Cl^-) respectively.

Microfluidic Electrochemical Detection System

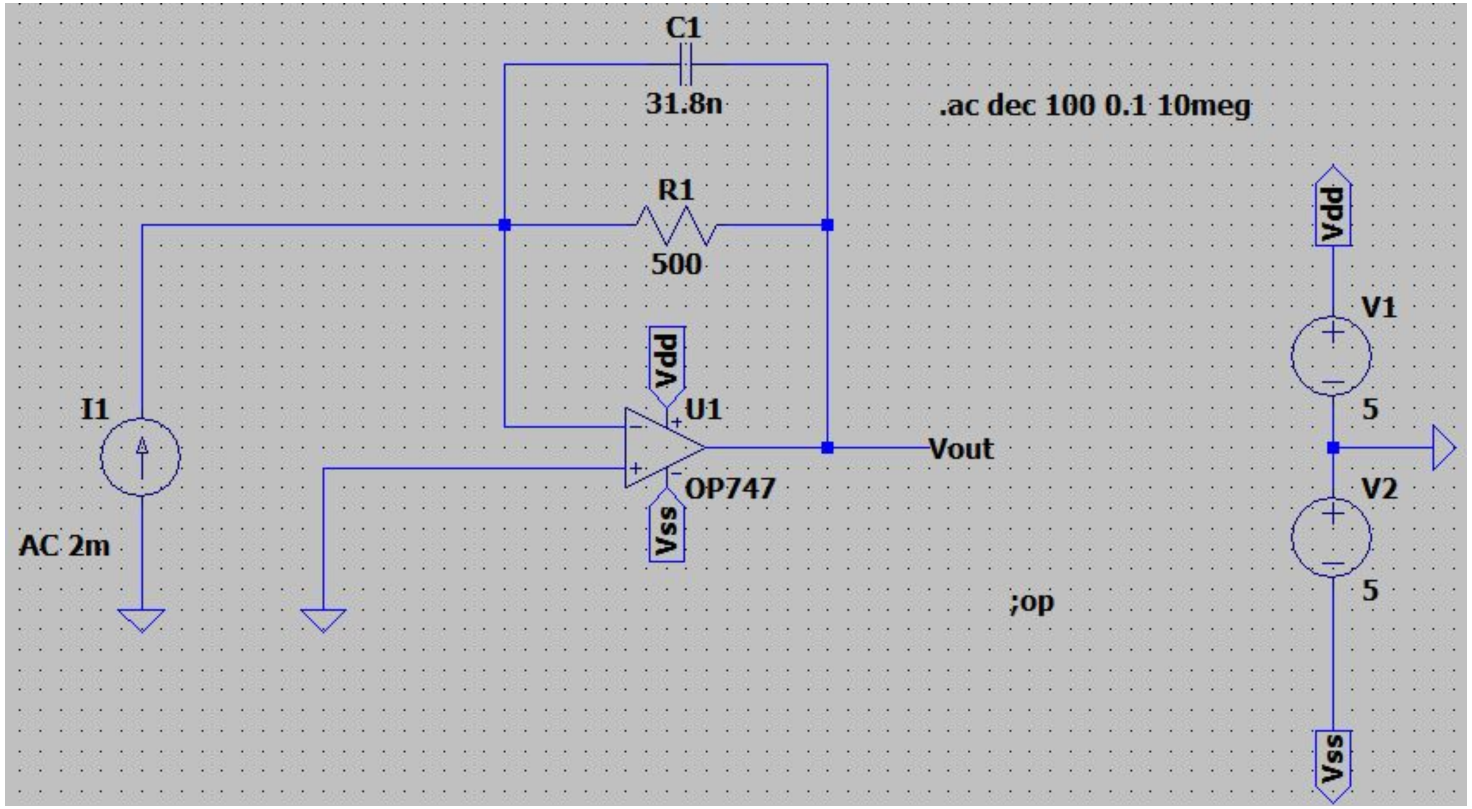
- The solid contact ion-sensitive electrodes (ISEs) for the detection of Na^+ and K^+ can be developed in two alternative formulations, containing either poly(3,4-ethylenedioxythiophene) (PEDOT) or poly(3-octylthiophene-2,5-diyl) (POT) as a conductive polymer transducing component.
- The solution-processable POT formulation simplifies the fabrication process, and sensor to sensor reproducibility can be improved via partial automation using an Opentron® automated pipetting robot.
- The resulting electrodes would show a good sensitivity (52.4 ± 6.3 mV/decade (PEDOT) and 56.4 ± 2.2 mV/decade (POT) for Na^+ ISEs, and 45.7 ± 7.4 mV/decade (PEDOT) and 54.3 ± 1.5 mV/decade (POT) for K^+) and excellent selectivity towards potential interferents present in human sweat (H^+, Na^+, K^+, Mg^{2+}, Ca^{2+}).

Amplifier Circuit

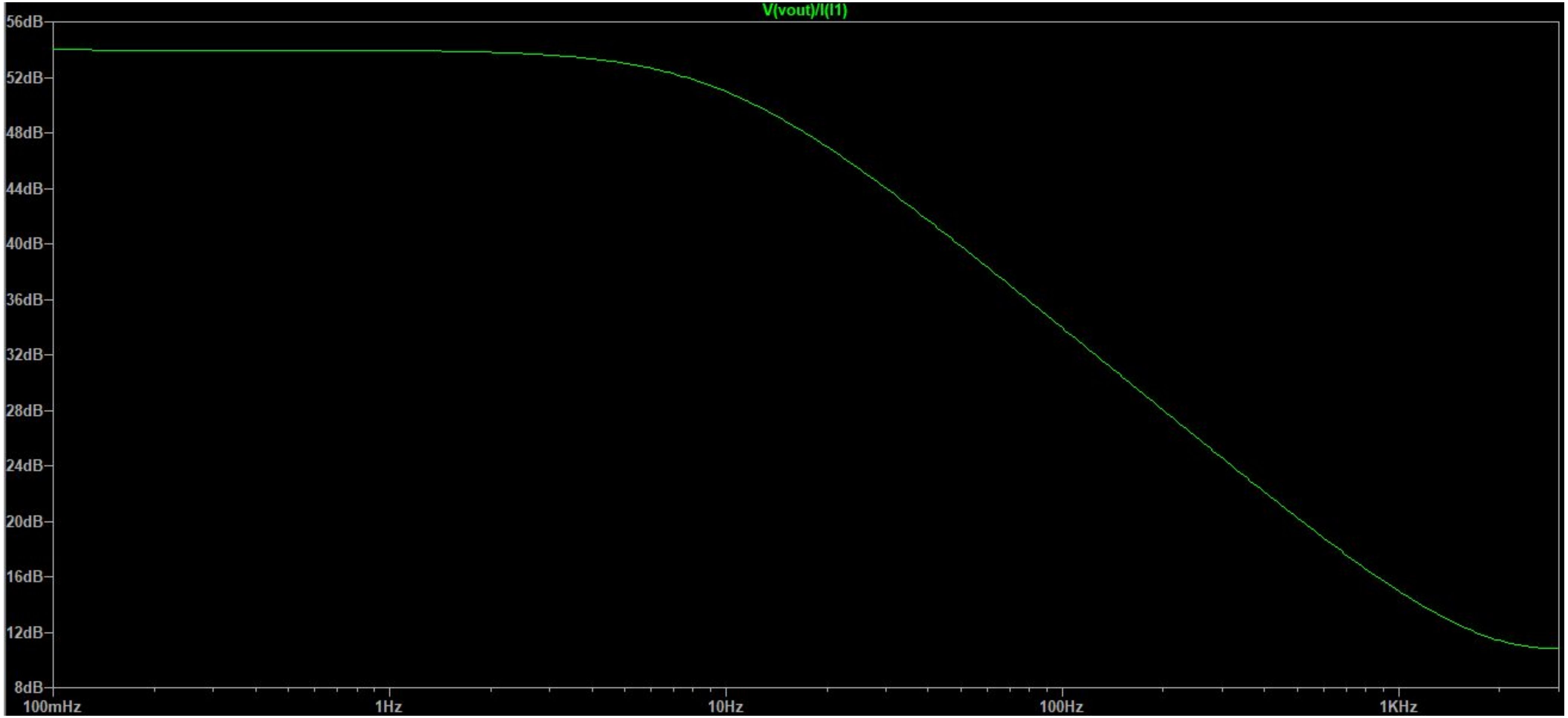
- 2 types of circuits will be used, one for the potentiometric sensing, and one for amperometric sensing.
- The glucose sensing will use the upper circuit shown
- The Na+ and Cl- will use the sensors shown below



Transimpedance Amplifier



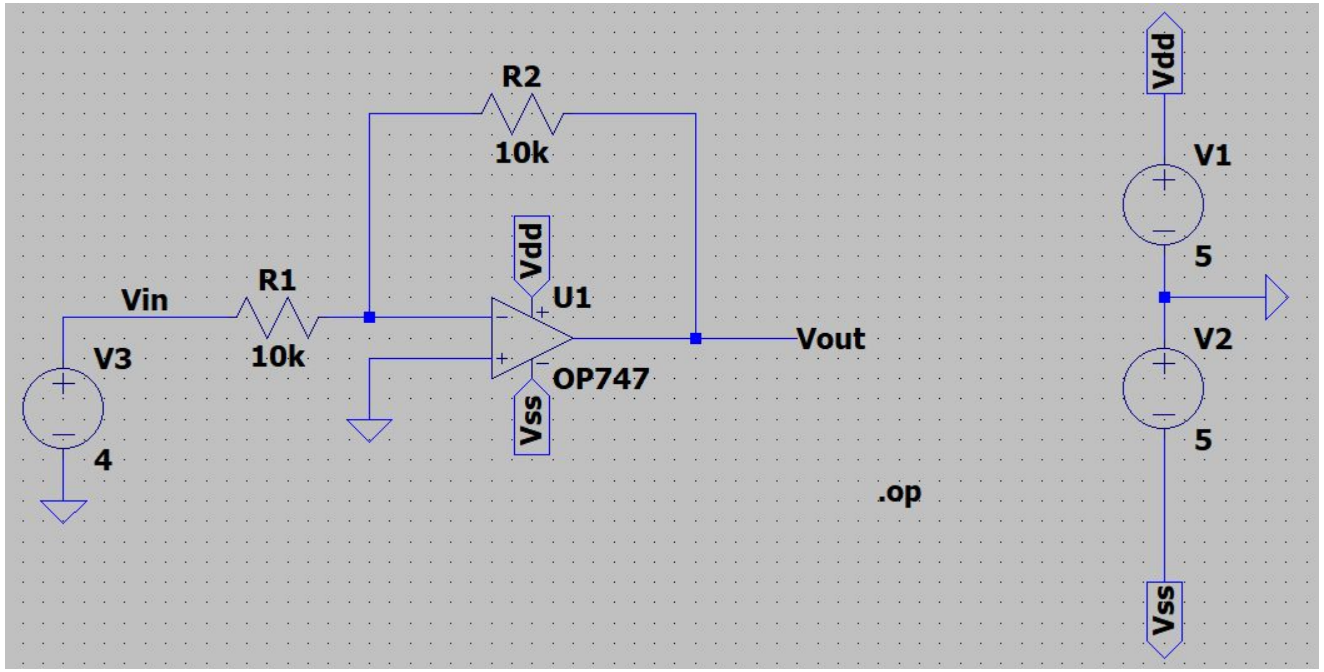
Gain vs frequency plot



Unity gain Inverter

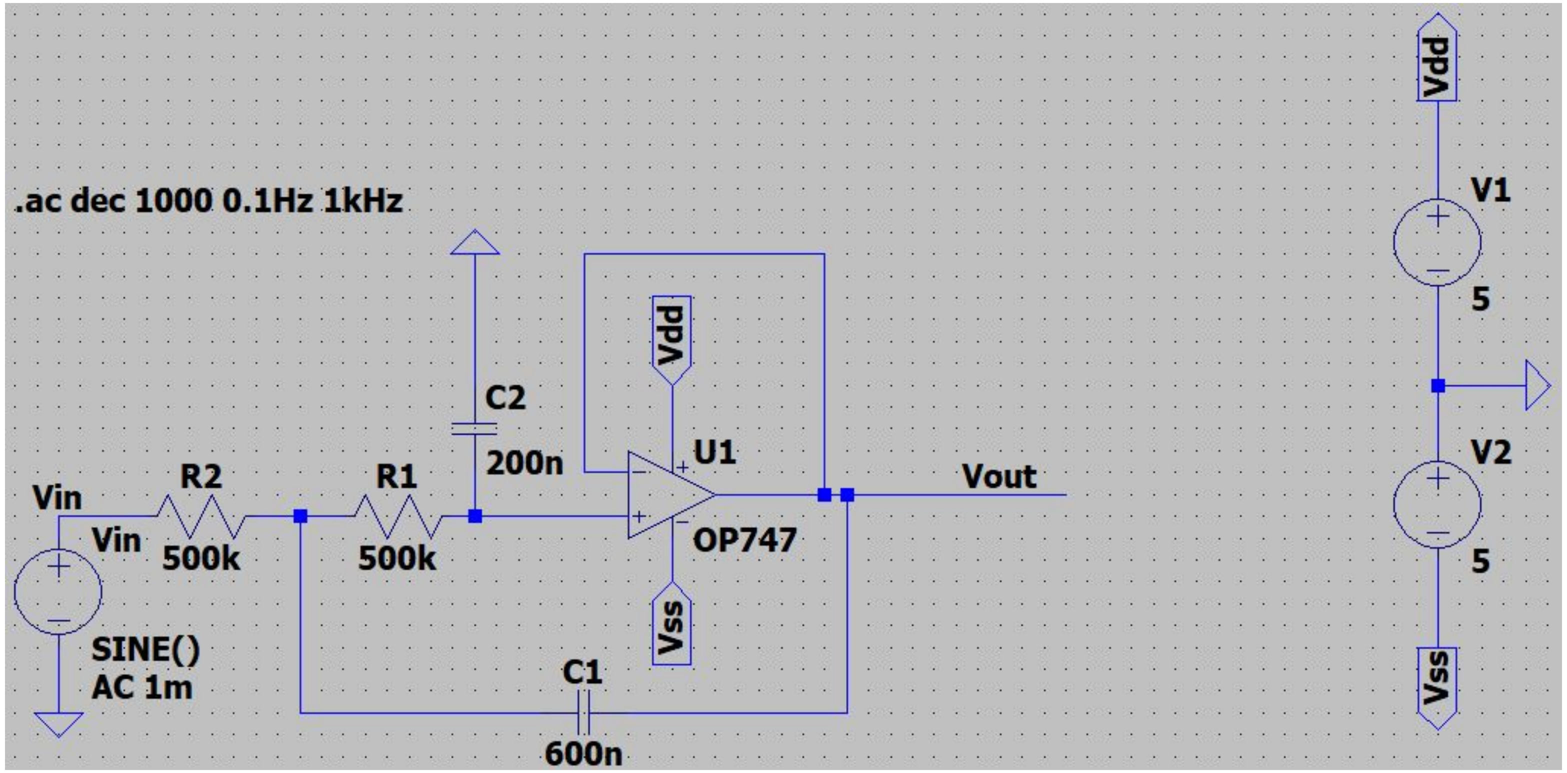
--- Operating Point ---

V(n001):	8.37724e-005	voltage
V(vss):	-5	voltage
V(vdd):	5	voltage
V(vout):	-3.99993	voltage
V(vin):	4	voltage
I(R2):	-0.000400001	device_current
I(R1):	-0.000399992	device_current
I(V3):	-0.000399992	device_current
I(V2):	-0.000507776	device_current
I(V1):	-0.000107796	device_current
Ix(u1:1):	-1.1599e-008	subckt_current
Ix(u1:2):	-9.5975e-009	subckt_current
Ix(u1:99):	0.000107796	subckt_current
Ix(u1:50):	-0.000507776	subckt_current
Ix(u1:45):	0.000400001	subckt_current

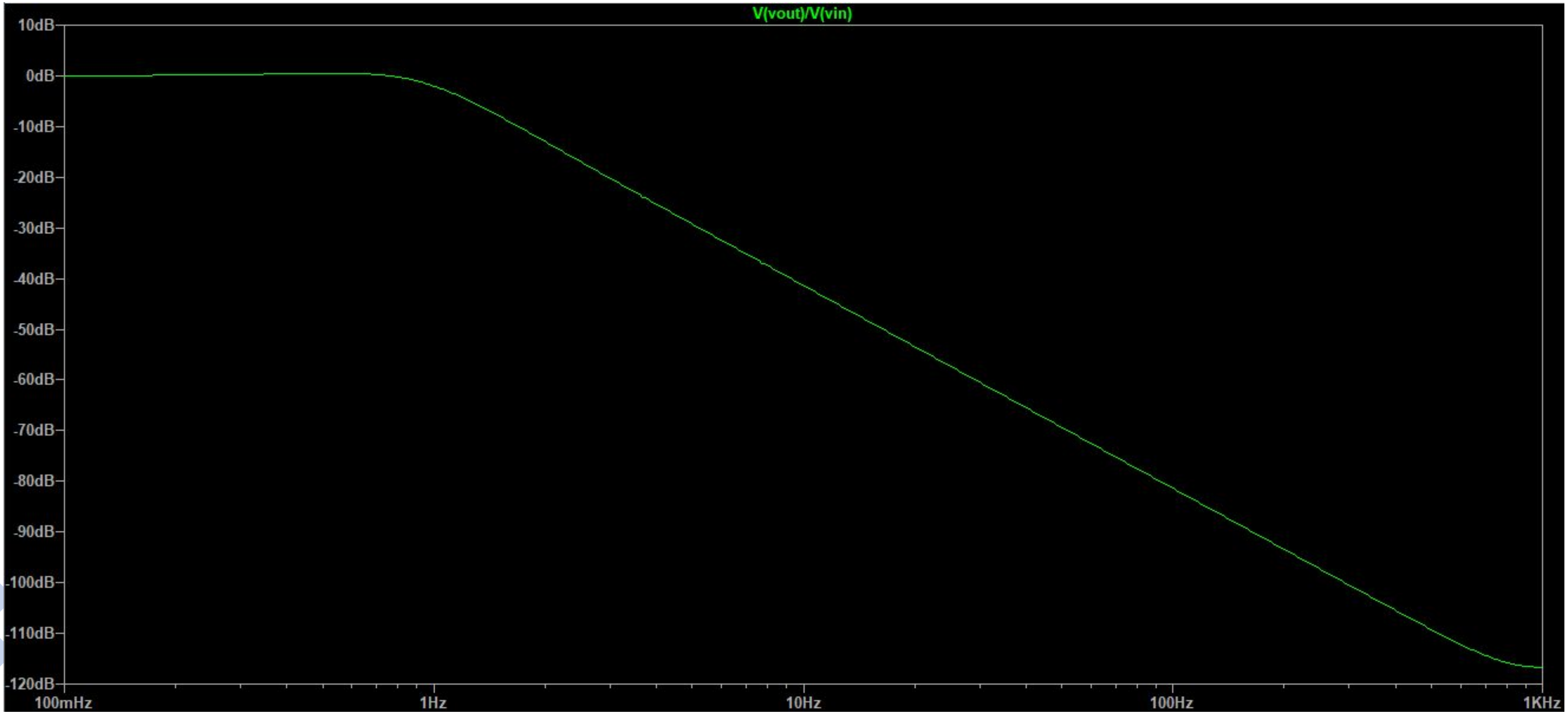


Unity Gain 2nd Order Low Pass Filter

- Sallen Key Topology



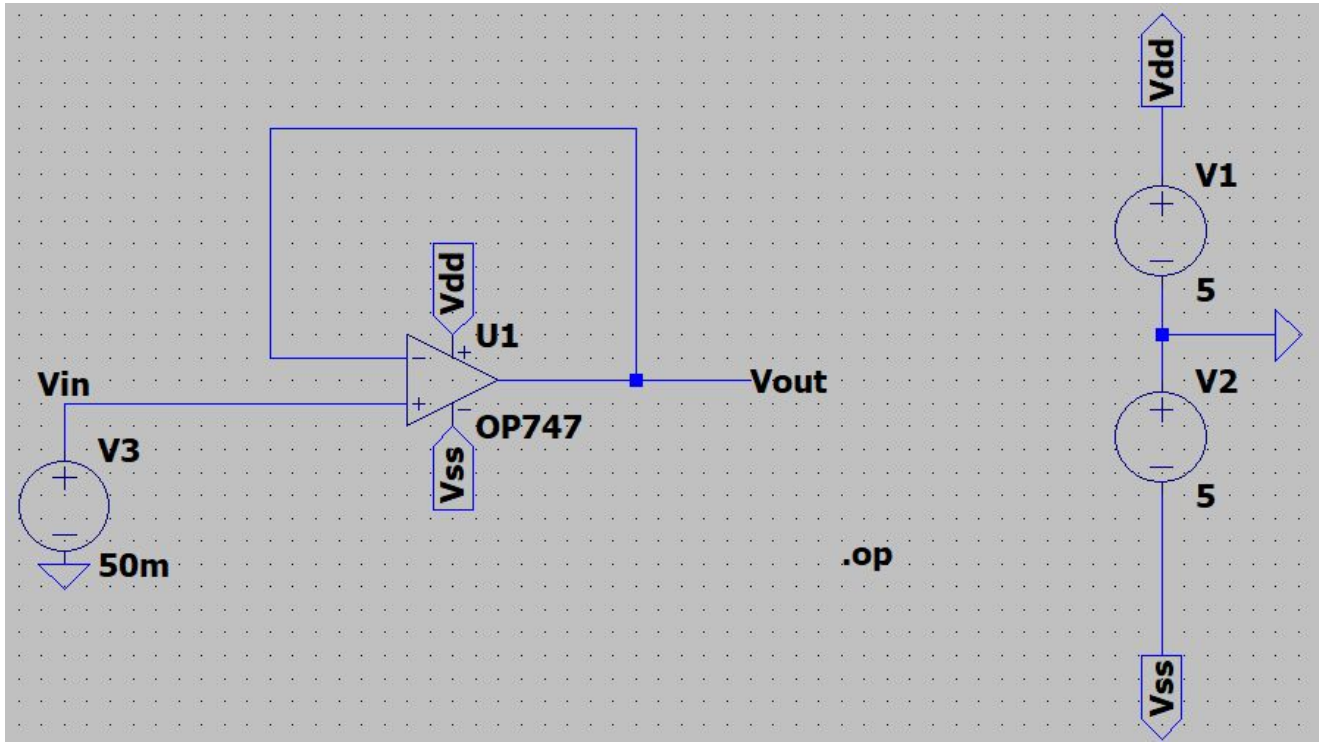
Gain vs frequency plot



Voltage Buffer

--- Operating Point ---

V(vout):	0.05008	voltage
V(vss):	-5	voltage
V(vdd):	5	voltage
V(vin):	0.05	voltage
I(V3):	1.15943e-008	device_current
I(V2):	-0.00023381	device_current
I(V1):	-0.000233822	device_current
Ix(u1:1):	-1.15943e-008	subckt_current
Ix(u1:2):	-9.59429e-009	subckt_current
Ix(u1:99):	0.000233822	subckt_current
Ix(u1:50):	-0.00023381	subckt_current
Ix(u1:45):	9.59429e-009	subckt_current



Voltage Amplifier

--- Operating Point ---

V(n001):	-0.249404	voltage
V(vss):	-5	voltage
V(vdd):	5	voltage
V(n002):	-0.249484	voltage
V(vout):	-0.4991	voltage
V(vin):	-0.224444	voltage
V(n003):	-0.274444	voltage
I(R4):	-2.49484e-005	device_current
I(R3):	-2.49696e-005	device_current
I(R2):	2.496e-005	device_current
I(R1):	2.496e-005	device_current
I(V3):	-2.496e-005	device_current
I(V2):	-0.000247871	device_current
I(V1):	-0.000222923	device_current
Ix(u1:1):	-1.16182e-008	subckt_current
Ix(u1:2):	-9.61812e-009	subckt_current
Ix(u1:99):	0.000222923	subckt_current
Ix(u1:50):	-0.000247871	subckt_current
Ix(u1:45):	2.49696e-005	subckt_current