EE-517: Bio-Nano-Chip Design

Solutions 12: Bio-CMOS interfaces in voltage scan

December 1, 2020

Problem 1

The Nernst equation for the redox process is

$$\mathrm{E} = \mathrm{E}^0 - \frac{\mathrm{RT}}{\mathrm{F}} \ln\left(\frac{[\mathrm{Red}]}{[\mathrm{Ox}]}\right) - \frac{2.3\,\mathrm{RT}}{\mathrm{F}}\mathrm{pH}. \tag{1}$$

The variation of potential due to a change of pH is

$$\Delta\mathrm{E} = -\frac{2.3\,\mathrm{RT}}{\mathrm{F}}\Delta\mathrm{pH}, \tag{2}$$

while the variation of potential due to a change in redox compound concentration from $[\mathrm{Red}]_0$ to $[\mathrm{Red}]_1$, at constant pH, is

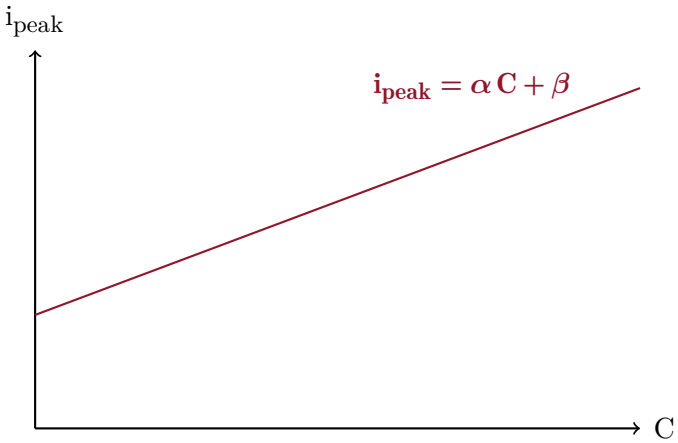
$$\Delta\mathrm{E} = -\frac{\mathrm{RT}}{\mathrm{F}} \ln\left(\frac{[\mathrm{Red}]_1}{[\mathrm{Red}]_0}\right). \tag{3}$$

By equating equations (2) and (3),

$$[\mathrm{Red}]_1 = [\mathrm{Red}]_0\, \mathrm{e}^{2.3\,\Delta\mathrm{pH}} = \mathbf{99.5\,mM}$$

Problem 2

We assume a linear relationship between the peak current and the concentration of the redox compound such that $\mathrm{i_{peak}} = \alpha\,\mathrm{C} + \beta$.



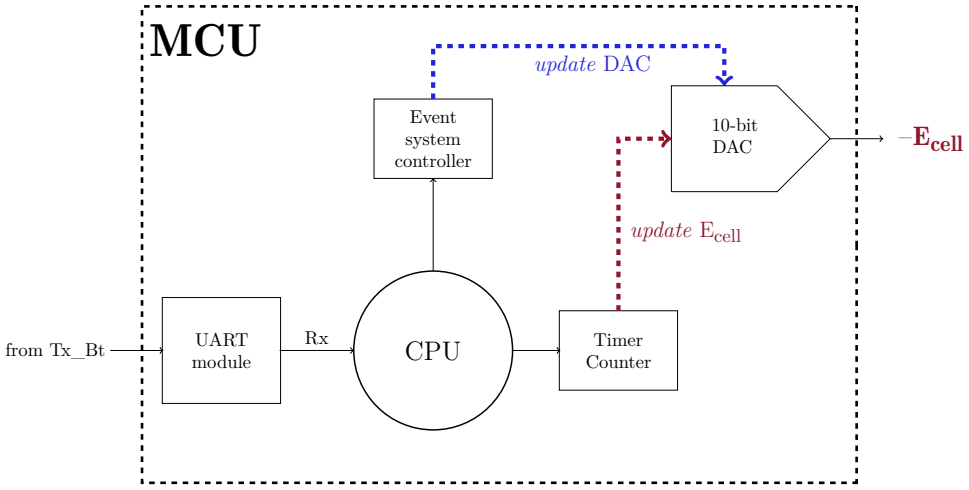
The coefficients α and β can be computed from the calibration data (system of 2 equations and 2 unknown), yielding $\alpha = 40\,\mu\mathrm{A}\cdot\mathrm{mM}^{-1}$, and $\beta = 72\,\mu\mathrm{A}$.

Thus, the concentration of the redox compound for a measured peak current $\mathrm{i_{meas}} = 92\,\mu\mathrm{A}$ is

$$\mathrm{C} = \frac{\mathrm{i_{meas}} - \beta}{\alpha} = \mathbf{500\,\mu M}$$

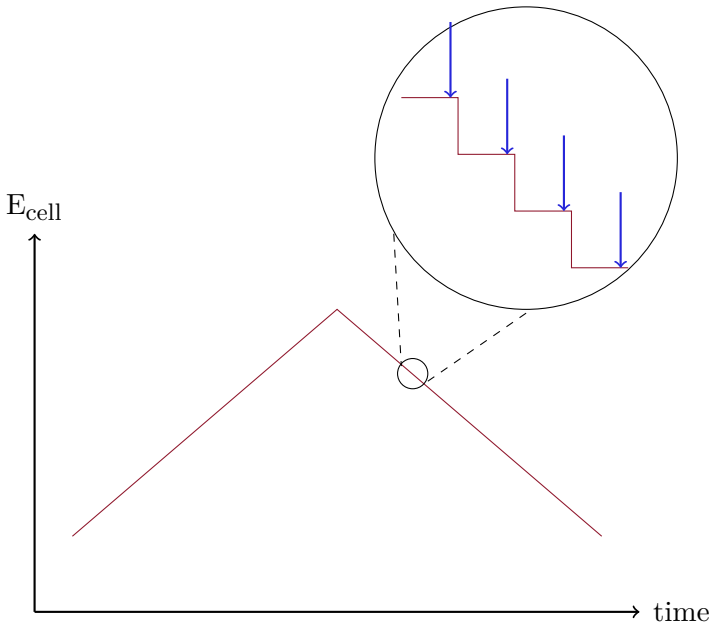
Problem 3

The electrochemical cell potential is scanned thanks to a *Direct Digital Synthesizer* (DDS) that outputs a staircase waveform, resulting in a triangular voltage scan. The system-level implementation of the DDS is illustrated hereunder.



The parameters of the DDS are conveyed by the user over an external serial communication link (from Bluetooth via the UART module in this case). These parameters are the voltage scan range $[E_{cell,start}; E_{cell,end}]$, the staircase width δt, and the staircase height δE. The DDS is implemented with a micro-controller unit, embedding a Timer/Counter module ensuring time synchronization, and a *Digital-to-Analog Converter* (DAC) that generates analog voltages to polarize the electrochemical cell. The DAC takes as input the value of E_{cell}, encoded as a digital word, and is refreshed by an event system controller once the Timer/Counter overflows.

Namely, at the beginning of operation, the digital word corresponding to $E_{cell,start}$ is fed to the DAC, and the Timer/Counter module is triggered, and starts counting (ramping up) until it overflows, after a period of δt. Once the Timer/Counter overflows, the digital word fed to the DAC is updated to $E_{cell,start} \pm \delta E$, and the Timer/Counter is reset and starts counting again. The DDS output is illustrated herein below, where the blue arrows indicate the instants where the Timer/Counter overflows, and E_{cell} is updated.



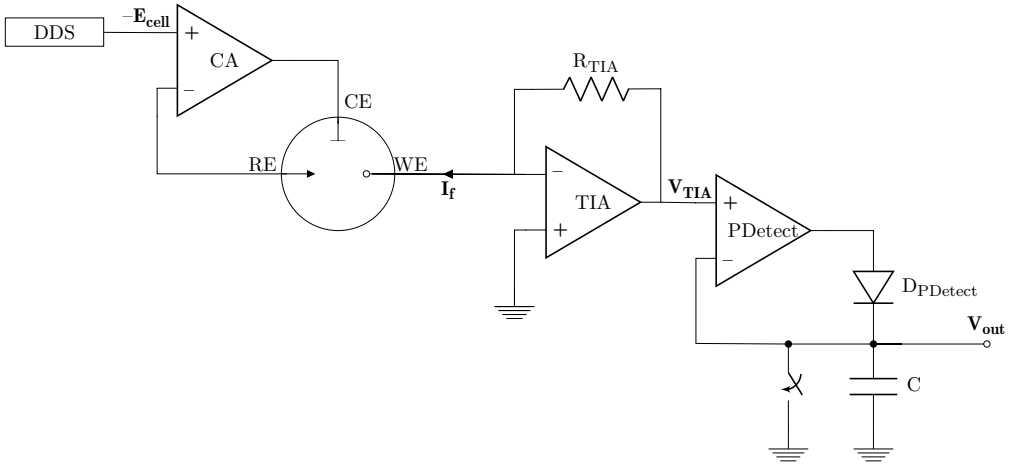
The voltage scan rate $\nu = \frac{\delta E}{\delta t}$ allows us to compute δt.

(a) the *Least Significant Bit* (LSB) of the DAC is the smallest value of δE that could be output by the DAC, $LSB_{DAC} = \frac{V_{cc}}{2^{10}-1} = 3.22\,mV$. In this case, $\boldsymbol{\delta t = \frac{LSB_{DAC}}{\nu} = 161\,ms}$.

(b) For $\delta E = 5\,mV$, $\boldsymbol{\delta t = 250\,ms}$.

Problem 4

(a) The front-end circuit is displayed hereunder.

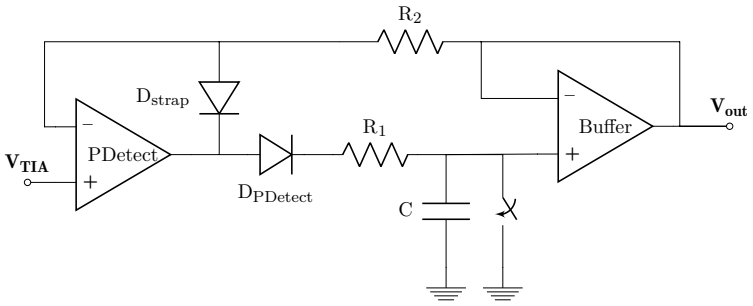


The DDS circuit discussed before outputs a voltage waveform $E_{cell}(t)$ that polarizes the electrochemical cell. The resulting faradaic current is sensed by the transimpedance amplifier as $V_{TIA}(t)$. This voltage signal exhibits two peaks explaining the oxidation of the two exogenous compounds. The peak voltages could be analysed with post-processing tools, but in this example, a peak detector circuit is asked to output the values of theses peak voltages.

An envelope detector could be obtained with a diode charging a capacitor. Opamp *PDetect* is added to avoid loading from the transimpedance amplifier while charging the capacitor. When V_{TIA} rises, the output of the opamp is positive, and the diode is forward-biased, allowing the charging of the capacitor. Once the peak $\hat{V}_{TIA}$ is reached, this voltage is decreasing, and the diode is reverse-biased. The value $\hat{V}_{TIA}$ is kept at V_{out}. A new sensing cycle is started by resetting the capacitor.

The above circuit has several shortcomings. First, if the load at the output of the capacitor is small, it could load C during charging phase, and the capacitor is discharged through this load during the hold phase of $\hat{V}_{TIA}$. Therefore, a buffering of the output is needed. Besides, during the holding phase, the opamp is in open-loop, so goes to saturation. It will need more time to get back in linear mode for further peak detection cycles.

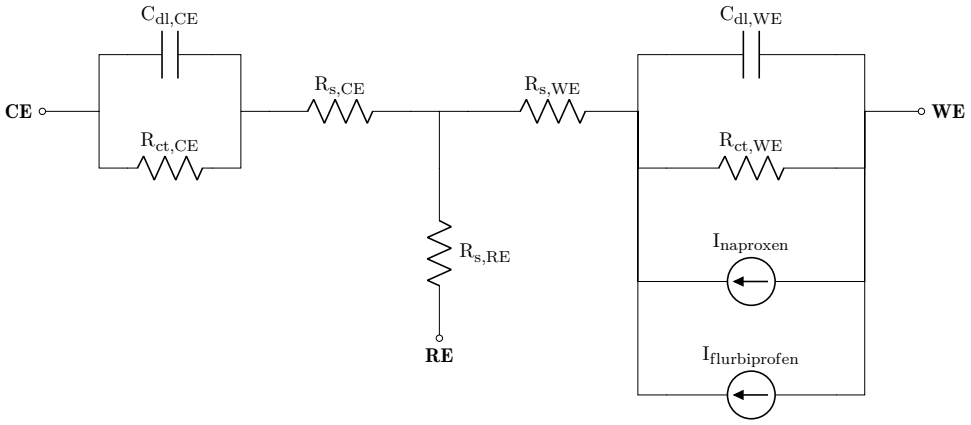
The following circuit could cope with these drawbacks.



When the output voltage of the transimpedance amplifier rises, the output of *PDetect* opamp is positive, so $D_{PDetect}$ is forward-biased, while D_{strap} is reverse-biased. The capacitor C is charged to $\hat{V}_{TIA}$, that is buffered to the output node by the *Buffer* opamp. Resistor R_1 prevents *PDetect* opamp from exceeding its short circuit output current, and limits overshoot if V_{TIA} is too fast for the opamp.

When V_{TIA} decreases so that the output of *PDetect* opamp is below $\hat{V}_{TIA} + V_d$, where V_d is the diode voltage drop, $D_{PDetect}$ diode is reverse-biased. Thus, the value at V_{out} is held at $\hat{V}_{TIA}$. Besides, the strap diode D_{strap} provides local feedback to *PDetect* opamp, therefore, avoids this opamp to go into saturation. The peak detector is in hold phase until the switch resets the capacitor, enabling subsequent peak detection.

(b) The Randles equivalent circuit is displayed hereunder



where the faradaic current is the sum of the currents accounting for the two different target metabolites in the solution, which are Naproxen and Flurbiprofen. The faradaic current is of the form

$$\mathrm{I_f} = \mathrm{I_{0,naproxen}}\, \mathrm{e}^{-\frac{(\mathrm{E_{cell}}-\mathrm{E_{0,naproxen}})^2}{\sigma_1^2}} + \mathrm{I_{0,flurbiprofen}}\, \mathrm{e}^{-\frac{(\mathrm{E_{cell}}-\mathrm{E_{0,flurbiprofen}})^2}{\sigma_2^2}},$$

where $\mathrm{I_0}$ is the peak current related to the redox compound concentration by Randles-Sevcik equation, and $\mathrm{E_0}$ is the redox potential of the electroactive compound ($\mathrm{E_{0,naproxen}} = 50\,\mathrm{mV}$, and $\mathrm{E_{0,flurbiprofen}} = 0\,\mathrm{mV}$).