EE-517: Bio-Nano-Chip Design

Exercises 13: Bio-CMOS circuits for DNA detection

December 8, 2020

Problem 1

Consider a *Charge-Based Capacitance Measurement* (CBCM) circuit. Evaluate the range of capacitance that could be sensed at the Bio/CMOS interface by a CBCM front-end designed with the hereunder specifications.

- *Square wave signal applied at the Bio/CMOS interface:*
  $\mathrm{V_{step}} = 100\,\mathrm{mV}$ duty_cycle $= 50\%$ $\mathrm{f} \in [10\,\mathrm{Hz}; 10\,\mathrm{MHz}]$
- *Resistance of the bio layer:* $\mathrm{R_{bio}} = 5\,\mathrm{M\Omega}$
- *Detectable current range:* $\mathrm{I_{avg}} \in [3.3\,\mu\mathrm{A}; 3.3\,\mathrm{mA}]$

Problem 2

Assume that the integration stage of the CBCM is implemented with an RC opamp-based integrator with DC gain control. Design this circuit block such that it could measure Bio/CMOS interface capacitance in the range of frequency $[10\,\mathrm{Hz}; 100\,\mathrm{kHz}]$.

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Problem 3

A circuit front-end for label-free DNA detection is considered. The sensing electrodes consist of two interdigitated gold electrodes bio-modified by covalent binding of single-stranded DNA probes. Hybridization events of complementary DNA strands (probe/target molecules) is detected by the variation of the interface capacitance. A capacitance-to frequency converter is implemented in Figure. 1.

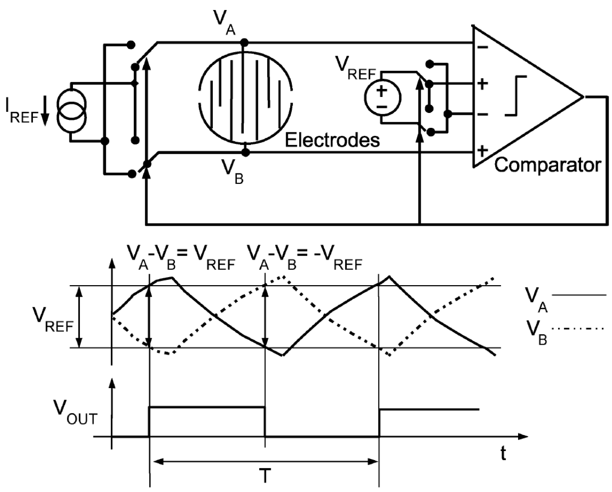

Figure 1: Capacitance-to-Frequency measurement circuit [1].

A periodic current excitation I_{REF} polarizes the electrodes. The electrodes respond to the stimulus by changing their voltage difference $V_C = V_A - V_B$, in a transient waveform which time constant is dominated by the capacitive elements of the electrode-solution impedance. The comparator inverts the polarization current when V_C reaches the threshold values $\pm V_{REF}$. Therefore, the width of the pulsed signal V_{OUT} at the output of the comparator encodes the interfacial capacitance.

(a) Demonstrate that the period of the square signal V_{OUT} could be expressed as

$$T = 2RC\ln\left(\frac{1}{1-\frac{V_{REF}}{RI_{REF}}}\right),$$

where R and C represent the contribution of the interface resistance and capacitance, respectively, of both electrode/solution interface. Neglect the solution resistance and the geometrical two-plates capacitance formed by the two electrodes.

(b) Evaluate the range of frequency at which the comparator switches its state, with the specifications listed hereunder:

- *Resistance of the bio-layer:* $R_{bio} \in [5\,M\Omega; 15\,M\Omega]$
- *Capacitance of the bio-layer:* $C_{bio} \in [20\,nF; 40\,nF]$
- *Reference current driving the cell:* $I_{REF} = 3\,\mu A$
- *Threshold value of the comparator:* $V_{REF} = 200\,mV$

Problem 4

What is the relative error made in the computation of the switching frequency of the comparator of problem 3, when assuming that $\frac{V_{ref}}{R_{bio}I_{ref}} \longrightarrow 0$?

References

[1] C. Stagni, C. Guiducci, L. Benini, B. Riccò, S. Carrara, B. Samorí, C. Paulus, M. Schienle, M. Augustyniak, and R. Thewes, "CMOS DNA sensor array with integrated A/D conversion based on label-free capacitance measurement," *IEEE Journal of Solid-State Circuits*, vol. 41, no. 12, pp. 2956–2963, 2006.