Ultra-Sensitive Radio Frequency Biosensor at an Exceptional Point of Degeneracy induced by time modulation

Hamidreza Kazemi, Amirhossein Hajiaghajani, Mohamed Y. Nada, Manik Dautta, Muhannad Alshetaiwi, Peter Tseng, and Filippo Capolino

Abstract—We exploit the premises of exceptional points of degeneracy (EPDs) induced in linear time-periodic (LTP) systems to achieve extremely sensitive biosensors. The EPD is formed in a single LC resonator where the total capacitance is comprised of a time-varying capacitor in parallel to a biosensing capacitor. We show the emergence of EPDs in such a system and the ultra sensitivity of the degenerate resonance frequency to perturbations. Moreover, we investigate the capacitance and conductance variations of an interdigitated biosensing capacitor to the changes in the concentration of a biological material under test (MUT), leading to subsequent large changes in the resonance frequency of the LTP-LC resonator. A comparison with a sensor based on a standard LC resonator demonstrates the ultra-high sensitivity of the proposed LTP-LC based biosensor. In addition, we show the scalability of the biosensor sensitivity across different frequency ranges.

I. INTRODUCTION

Analytical biosensors play a tremendous role in modern medicine through enabling the monitoring of biomarkers in human health. The applications of these sensors are diverse as they form the core of many point-of-care, wearable, and diagnostic tools utilized in pathology, nutrition, fitness, biomedical science, and more [1, 2, 3, 4, 5]. Traditionally, an analytical biosensor is composed of two main elements: a bioamplifier (such as a bioreceptor), and a transducer (converting the biological signal into an electrical one). Various number of modalities exist to monitor biomarkers [6, 7], including but not limited to electrochemical impedance spectroscopy [8, 9, 10], piezoelectric microcantilever [11, 12, 13], surface plasmon resonance [14, 15, 16, 17], immunoelectrophoresis [18, 19], fluorescence [20, 21], enzyme-linked immunosorbent assay (ELISA) [22, 23, 24, 25]. While many of these techniques have found critical roles in a variety of applications, a majority are encumbered by limitations in system size and weight, sample preparation requirements, power consumption, and limited capabilities in wireless operation.

Dielectric-RF sensors (that sense the presence of analytes via permittivity shifts) possess traits that address many issues that have limited traditional biosensors, however these sensors have limited use in modern devices. The reason for this is two-fold: these sensors possess low sensitivity (signal change due to input) and low selectivity (discrimination of an analyte from interferents). While there are potential strategies to improve RF-biosensor selectivity [26], here we examine a new electromagnetic amplification strategy to improve biosensor sensitivity.

One of the most recent methods to dramatically enhance biosensors sensitivity is to design the RF sensor to operate at the so called exceptional point of degeneracy (EPD). The EPD represents the coalescing point of the degenerate resonance frequencies and it emerges in a system when two or more eigenmodes of the system coalesce into a single degenerate eigenmode in both their eigenvalues and eigenvectors [27, 28, 29, 30, 31, 32, 33]. The system at an EPD shows an inherent ultra sensitivity, specially for small perturbation, that can be exploited to enhance the sensitivity of the liquid-based radio frequency biosensor [34, 35, 36, 37, 38, 39]. In addition to high sensitivity, EPDs are associated with other unique properties such as enhancing the gain of active systems [40], lowering oscillation threshold [41], etc.

Recently, EPD associated sensors based on the concept of parity-time (PT) symmetry in multiple, coupled resonators have been investigated in Refs. [42, 43, 44]. In this paper, instead, we use the new concept of an EPD that occurs in a single resonator and it is not based on PT-symmetry [34]; this

Figure 1. The proposed sensor circuit working at an exceptional point of degeneracy consisting of a time-varying LC resonator in parallel to a biosensing capacitor (its capacitance is function of the concentration of the material under test (MUT)). The biosensing capacitor is realized using an interdigitated capacitor. The EPD induced in this single linear-time-periodic (LTP)-LC resonator is responsible of the very high sensitivity.

H. Kazemi, A. Hajiaghajani, M. Y. Nada, M. Dautta, M. Alshetaiwi, P. Tseng, and F. Capolino are with Department of Electrical Engineering and Computer Science, University of California, Irvine, CA 92697, USA (e-mail: {hkazemiv,ahajiagh,mynada,mdautta,malsheta,tsengpc,f.capolino}@uci.edu).

P. Tseng is also with the Department of Biomedical Engineering, University of California, Irvine, CA 92697, USA.
new method is used to generate a second order EPD induced by time-periodic variation of a system parameter [34] aiming at improving the sensitivity of liquid based radio frequency biosensors, leading to an intrinsic ultra sensitivity. The concept of an EPD in a single resonator obtained by simply applying a time domain modulation which was shown in Ref. [34], and the experimental demonstration of the occurrence of such EPD has been shown in Ref. [45]. In this paper we apply the EPD concept developed in these two papers to conceive a new class of biosensors. The proposed biosensor shown in Fig. 1 is comprised of an LC resonator where the capacitor is time-varying and is in parallel to the biosensing capacitor, i.e., the capacitor whose capacitance is function of the concentration of the material under test (MUT). The biosensing capacitor is implemented using an interdigitated capacitor (IDC) as shown in Fig. 1. In this system, the change in the concentration of the MUT will change the capacitance of the IDC that can be measured through the shift in the resonance frequency of the system and this shift is boosted when the system operates at an EPD. We study two different biosensing scenarios based on the IDC in Fig. 1 (i) a uniformly dissolved MUT in the background material above the IDC, and (ii) a thin layer of MUT placed on top of the electrodes which are denoted by A and B in Fig. 1.

In the following, we first show the behavior of a linear time periodic (LTP) LC resonator through the dispersion relation of the resonance frequency versus modulation and we discuss the occurrence of EPDs in such a system. The analysis accounts for losses in the system. In section III we design and investigate the performance of an IDC which is integrated in the system as the biosensing capacitor. We show the effect of the concentration of the MUT on the capacitance and the conductance of such capacitor for two cases of uniformly dissolved MUT and effective MUT layer. Finally, in section IV, we show the sensitivity of the designed system to perturbation, i.e., the concentration of the MUT, and we characterize the proposed biosensor performance across different designs and frequencies. Moreover, to show the advantages and the superiority of the proposed EPD biosensor, we compare its sensitivity with that of conventional biosensors.

II. ENHANCING THE SENSITIVITY OF BIOSENSORS IN AN LTP SYSTEM WITH EPDs

In this section, we demonstrate how to boost the sensitivity of conventional biosensors using a LTP-LC resonator as indicated in Fig. 2(a) where the time-periodic variation is introduced in the system through the time-varying capacitor, \( C_{ltv}(t) \). The two-dimensional state vector \( \Psi(t) = [q(t), i(t)]^T \) describes this system, where \( T \) denotes the transposaper operator, \( q(t) \) and \( i(t) \) are the capacitor charge on both the capacitors in Fig. 2(a) and inductor current, respectively. The temporal evolution of the state vector obeys the two-dimensional first-order differential equation [34]

\[
\frac{d}{dt} \Psi(t) = M(t) \Psi(t) \tag{1}
\]

where \( M(t) \) is the \( 2 \times 2 \) time-varying system matrix. Assuming that the time-variation of the capacitance is a two level piece-wise constant, periodic, function as shown in the subset of Fig. 2(a), the time-variant system matrix reads

\[
M_p = \begin{bmatrix}
-G_{bio}/(C_p+C_{bio}) & -1 \\
1/(L_0(C_p+C_{bio})) & -R/L_0
\end{bmatrix},
\tag{2}
\]

where \( C_p \), with \( p = 1, 2 \), represents the two values of the piece-wise constant time-varying capacitance \( C_{ltv}(t) \) and \( C_{bio} \) is the capacitance of the biosensing capacitor. The linear time-varying capacitance \( C_{ltv}(t) \) is \( C_{ltv} = C_1 \) for \( 0 < t \leq 0.5T_m \) and \( C_{ltv} = C_2 \) for \( 0.5T_m < t \leq T_m \). Losses in the system are represented by the series resistance of the inductor \( R \) and the parallel conductance \( G_{bio} \) of the biosensing capacitor. The conductance \( G_{bio} \) represents losses in the background medium and in the MUT.

Considering that the LTP sensor is periodic with period \( T_m = 1/f_m \), we can translate the state vector from the time instant \( t \) to \( t + T_m \) as \( \Psi(t + T_m) = \Phi(t, t + T_m) \Psi(t) \) through the \( 2 \times 2 \) state transition matrix \( \Phi(t, t + T_m) \) [34] [46]. In addition, the state vector satisfies \( \Psi(t + T_m) = e^{i\omega T_m} \Psi(t) \) in a periodic systems, hence we constitute the eigenvalue problem as

\[
(\Phi(t, t + T_m) - e^{i\omega T_m} I) \Psi(t) = 0,
\tag{3}
\]

where \( I \) is the \( 2 \times 2 \) identity matrix. Considering the eigenvalue problem derived in (3), we find the eigenvalues \( e^{i\omega T_m} \) of the state transition matrix \( \Phi(t, t + T_m) \), hence the circuit eigenfrequencies \( f = \omega/(2\pi) \) that are the resonance frequencies of the circuit. Figure 2(b) shows the dispersion of these LTP-LC resonant frequencies versus modulation frequency \( f_m \).
The small asymmetry of the real and imaginary parts of the resonance frequencies \( f \) with respect to the center \( f = 0 \) is due to the small losses in the circuit components. Such a dispersion diagram is obtained for the circuit parameters set as \( L_0 = 15 \mu \text{H}, R = 0.12, \) \( C_1 = 4.5 \text{nF}, C_2 = 1.5 \text{nF.} \) The parameters of the biosensing capacitor are derived based on the first order model described in Section III and set as \( C_{bio} = 0.3 \text{nF and } G_{bio} = 67 \mu \text{S.} \) It is observed from Fig. 2(b) that the time-periodic LC resonator exhibits second order EPDs (the band edges of each band gap) for selected modulation frequencies, i.e., when two resonance frequencies coalesce at a specific modulation frequency \( f_m \). Note that the LC resonator is time-periodic, therefore for a resonance frequency \( f \) there exist all the correspondent Fourier harmonics \( f + n f_m \), where \( n = \pm 1, \pm 2, ... \). The EPDs occur either at the center or at edge of the Brillouin zone (BZ) (we use this term in analogy to what happens in periodic electromagnetic waveguides \([39]\)) as it can be inferred from Fig. 2(b). For instance, one of the EPDs in Fig. 2(b) is indicated with a black circle: at the modulation frequency \( f_m = 112.6 \text{kHz} \) the LTP-LC resonance frequencies are \( f_e = f_{e0} + n f_m \). The one in the black circle corresponds to the \( n = 0 \) harmonic \( f_{e0} = 2.6 \text{kHz} \), and the small imaginary part is due to losses in the circuit.

The resonance frequencies of such a system operating at an EPD are highly sensitive to perturbation of any system parameter. In general, a perturbation \( \delta \) leads to a perturbed transition matrix parameter. In general, a perturbation \( \delta \) to an EPD are highly sensitive to perturbation of any system part is due to losses in the circuit.

An IDC is considered here as a reliable candidate to realize the biosensing capacitor \( C_{bio} \). The capacitance and conductance of the IDC depend on the geometrical design and the electromagnetic properties of the various materials used to fabricate the capacitor. We propose an equivalent circuit model for the IDC that easily describes the sensor’s port admittance as shown in Fig. 3 and that will be used for the perturbation analysis in the next subsection.

In order to simplify the analysis of the IDC and obtain an equivalent circuit model, we divide the media surrounding the electrodes into several domains based on their electromagnetic properties and electric field distribution. Hence, we model each domain by a parallel capacitance and conductance, placed along the direction of the electric field. The cross section of the biosensing capacitor showing the different domains is illustrated in Fig. 3(a) where only two electrodes of the interdigitated capacitor are shown. The domains are the substrate, the inter-electrode layer, and the background material above the electrodes. The equivalent circuit models of such domains are in parallel (see Fig. 3(a)). In practice, the background and the substrate domains are significantly thicker than the inter-electrode gap, hence they are approximated by two infinite half-spaces. The fringing electric field distribution between two electrodes of the IDC cell is similar to that of a pair of parallel strip lines. We derive analytical formulas for capacitances and conductances of the equivalent circuit model of the cell shown in Fig. 3(a) by fitting the result of the admittance formula of two parallel strip lines to that of numerical simulations. The numerical results are obtained by finite element method (FEM) simulations implemented in COMSOL Multiphysics® \([39]\). Typically, the geometrical ratios in strip lines are different from IDC, and to derive accurate ad-hoc formulas, we add correction factors in the analytic expressions for the capacitance and conductance of the parallel strip lines (whose approximation is available in \([50]\)):

\[
C_b = \frac{\varepsilon_0 \varepsilon_r \pi L_c}{\ln \left( 4 \left( \alpha_1 + d_c/w_c \right) \right)} \quad (5)
\]

\[
G_b = \frac{\sigma_b L_c}{\alpha_2 + \alpha_3 \cosh^{-1}(1 + d_c/w_c)}, \quad (6)
\]

where \( L_c \) and \( w_c \) represent the length and width of each electrode, respectively, \( d_c \) is the gap between the two adjacent electrodes, \( \varepsilon_{rb} \) and \( \sigma_b \) are the relative permittivity and the conductivity of the background medium, respectively, and \( \varepsilon_0 \) is the permittivity of vacuum. We anticipate that the constant coefficients \( \alpha_1 = 0.46, \alpha_2 = 0.21 \) and \( \alpha_3 = 0.58 \) are obtained from the fitting procedure based on the IDC parameters given hereafter for the IDC biosensor shown in Fig. 1.

Note that the equivalent capacitance and conductance of the substrate domain are derived from \( (5) \) and \( (6) \), simply by replacing the background material parameters with those of the substrate, i.e., replacing \( \varepsilon_{rb} \) and \( \sigma_b \) with \( \varepsilon_{rs} \) and \( \sigma_s \), respectively.

We assume that the inter-electrode domain is filled with the background material and due to the small (compared to the wavelength) parallel side walls of the adjacent electrodes, the inter-electrode domain experiences a uniform electric field distribution, hence the equivalent capacitance and conductance of the inter-electrode domain are estimated by \([51]\).
Geometrical parameters are set as the IDC using (5)-(8). For the aforementioned design, the interdigitated capacitor is approximated as a reasonable approximation, the admittance of a single cell of the IDC at its terminals in the considered frequency range. With a negligible inductance range and also due to the parallel connection of the electrodes, the cells are in parallel. According to the operative frequency x repeated in the N domain, respectively. The IDC is comprised of the relative permittivity, and conductivity of the inter-electrode background material where \( \delta = 0 \) represents the unperturbed structure (i.e., only the background material is present) and \( \delta = 1 \) means that the entire background material is replaced by the MUT. Such a uniform mixture of the MUT and background material can be described by an effective permittivity and conductivity using the linear mixture formula for composite media \( 53, 54, 55 \).

\[
\frac{\varepsilon_{\text{eff}}}{\varepsilon_0} = \delta \varepsilon_{\text{rm}} + (1-\delta)\varepsilon_{\text{rb}} \tag{9}
\]

\[
\frac{\sigma_{\text{eff}}}{\sigma_{\text{m}}} = \delta \sigma_{\text{m}} + (1-\delta)\sigma_{\text{b}}, \tag{10}
\]

where \( \varepsilon_{\text{rm}} \) and \( \sigma_{\text{m}} \) represent the relative permittivity and conductivity of the MUT, respectively.

To find the equivalent capacitance and conductance of the first biosensing scenario in Fig. 4(a), we substitute the effective parameters of the composite mixture formula (9) and (10) into (5) and (6) to derive the equivalent circuit parameters of the perturbed biosensor capacitor \( C_{\text{bio}} \) shown in Fig. 4(a). The change in the capacitance and conductance values of the perturbed equivalent circuit biosensor capacitor \( C_{\text{bio}} \) and \( G_{\text{bio}} \) are respectively denoted by \( \delta C_{\text{bio}} = (C_{\text{bio}}(\delta)-C_{\text{bio}})/C_{\text{bio}} \) and \( \delta G_{\text{bio}} = (G_{\text{bio}}(\delta)-G_{\text{bio}})/G_{\text{bio}} \) are reported in Fig. 4(c). The result in this Figure is based on the assumption that the MUT is glucose described with \( \varepsilon_{\text{rm}} = 30 \) and \( \sigma_{\text{m}} = 0.6 \mu S/\mu m \) in the considered frequency range \( 56 \).

In the second biosensing scenario, Fig. 4(b), we consider a thin MUT layer (i.e., typically a protein layer) with relative volumetric concentration \( \delta \), that adheres to the top surface of the electrodes and is surrounded by the background material as shown in Fig. 4(b). Therefore, a layer made of MUT and background material is formed (referred to as effective MUT in the following) and it covers the entire electrodes’ surface through which the fringing electric field passes. Hence, the effective layer is modeled by a circuit comprised of a capacitance \( C_{\text{MUT}} \) in parallel with a conductance \( G_{\text{MUT}} \), where such circuit in turn is in series with the background domain’s equivalent circuit. Since the effective MUT layer thickness \( t_{\text{m}} \) is only a few nanometers, the electric field distribution is uniform in the this layer. The equivalent circuit parameters of the

\[
t_s = 0.3 \text{ nF}
\]

\[
t_e = 0.6 \mu S/\mu m 
\]

\[
t_s = 50 \mu m, \quad d_e = 250 \mu m, \quad \text{and} \quad N = 20. \quad \text{We use deionized water with} \quad \varepsilon_{\text{rb}} = 81.2, \quad \text{and} \quad \sigma_b = 5 \mu S/\mu m (\text{at} \ 100 \ MHz) \quad \text{as background and inter-electrode materials, and quartz with} \quad \varepsilon_{\text{rs}} = 4, \quad \sigma_s = 0 \text{ as substrate. The frequency dependent behavior of the materials is considered using the Debye model in Ref. [52].}

Next, we investigate the variation of the capacitance and conductance of the IDC based on the variation of the MUT concentration by using the derived model. According to the type of the MUT, there are two common biosensing modes: (i) the MUT (e.g., glucose) dissolves in the background material uniformly changing the electromagnetic properties of the background material, and (ii) a thin layer of the MUT (e.g., proteins) covers the exposed surface of the electrodes. The cross section of the perturbed biosensing capacitors for both sensing scenarios are depicted in Fig. 4(a) and (b), respectively.

The perturbation \( \delta \) in each biosensing scenario is defined as the relative volumetric concentration of the MUT in the background material where \( \delta = 0 \) represents the unperturbed structure (i.e., only the background material is present) and \( \delta = 1 \) means that the entire background material is replaced by the MUT. Such a uniform mixture of the MUT and background material can be described by an effective permittivity and conductivity using the linear mixture formula for composite media \( 53, 54, 55 \).

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effective MUT layer is obtained from $C_{MUT} = \varepsilon_{eff} \varepsilon_r L_e / t_m$ and $G_{MUT} = \sigma_{eff} \varepsilon_r L_e / t_m$, where $\varepsilon_{eff}$ and $\sigma_{eff}$ are given by the linear mixture formula in (9) and (10), respectively. Considering the equivalent circuit model of different domains represented in Fig. 4(b), we derive the variation in the values of the perturbed equivalent circuit parameters $C_{bio}$ and $G_{bio}$ ($\delta C_{bio}$ and $\delta G_{bio}$) reported in Fig. 4(d). The result in this figure is based on the assumption that the MUT is made of Keratin with $\varepsilon_{rm} = 8$ and $\sigma_m = 1.2 \mu S/m$, $t_m = 50 \text{nm}$.[57].

IV. CHARACTERIZATION OF THE BIOSensor PERFORMANCE

We characterize the sensitivity of the biosensor system operating at an EPD, based on a LTP-LC resonator made of the parallel arrangement of the biosensing capacitor in section III and a time-varying capacitor.

A. Sensitivity comparison with conventional biosensors

We start by showing a comparison between the sensitivity of a biosensor based on a LTP-LC resonator operating near an EPD and a conventional biosensor based on a linear time-invariant (LTI)-LC resonator, i.e., a standard LC resonator. The values of the LTP-LC resonator are the same as those in the previous sections. To assess a fair comparison, we assume that the capacitance in the LTI-LC resonator is equal to the time average capacitance in the LTP-LC resonator, i.e., $C_0 = (C_1 + C_2)/2$, and all the other parameters are the same as those of the LTP-LC case in Section II, i.e., $L_0 = 15 \mu H$, $R = 0.1 \Omega$, $C_{bio} = 0.3 \text{nF}$ and $G_{bio} = 67 \mu S$.

Figure 5 illustrates the change in the real part of a resonance frequency $\Delta f = f_p(\delta) - f_p(0)$ versus relative perturbation $\delta C_{bio}$, for both the LTI (standard case) and LTP (EPD case) biosensors. Therefore, for the LTP-LC biosensor, $\Delta f$ describes the shift of the resonance frequency $f_p(\delta)$ in the perturbed biosensor with respect to the 6th harmonics $(n = 6)$ of the degenerate resonance frequency, i.e., $f_p(0) = f_{e0} + 6f_{m} = 675.8 + j2.6 \text{ kHz}$ of the unperturbed biosensor (i.e., working at an EPD). Similarly, $\Delta f$ for the LTI-LC case shows the shift of the resonance frequency with respect to unperturbed resonance frequency $f_p(0) = (715.4 + j2.2) \text{ kHz}$. The change $\delta C_{bio}$ in the biosensing capacitance is due to the change in the MUT concentration $\delta$ in the background material, shown in Figs. 4(c) and (d) for the two biosensing scenarios.

The change of the resonance frequency $\Delta f = f_p(\delta) - (f_{e0} + 6f_m)$ based on the EPD perturbation is well described by the Puiseux series in [4], truncated to the first order. Indeed this approximation is in very good agreement with the “exact” result for the LTP case obtained by solving Eq. (3), showing the analytical nature of the ultra-sensitivity concept of the EPD-based sensor. In Fig. 5 we have normalized the perturbation of the resonance frequency for both the LTP-LC and LTI-LC resonators to the resonance frequency of the lossless unperturbed LTI-LC resonator that is calculated as $f_{LTI} = 1/(2\pi \sqrt{L_0(C_0 + C_{bio})}) = 715.4 \text{ kHz}$. This Figure shows the highly remarkable sensitivity associated with the biosensor designed to operate at an EPD of the LTP-LC system. Such ultra-sensitivity of the LTP-LC resonator operating
at a second order EPD was observed experimentally in \[45\] in general terms, hence here we investigate the sensitivity to the variation of a MUT in a biosensing scenario. One may note that the value of \(\alpha_1\) in Eq. (4) can significantly affect the sensitivity of the LTP-LC resonator and it is determined by the parameters of the system. Considering the values used in this paper, \(\alpha_1 = -j2.6\). Moreover, it can be inferred from the fractional power expansion of the resonance frequencies in Eq.(4) that for an imaginary value of \(\alpha_1\), a perturbation \(\delta > 0\) implies that only the real part of the resonance frequency changes while the imaginary part is constant (i.e. there are two purely real frequencies), whereas a perturbation \(\delta < 0\) implies that the imaginary part is the one changing while the real part remains constant. Future work shall focus on how to maximize this value based on the design of the circuit parameters.

### B. Sensing scalability across different frequencies

As mentioned in the introduction, a system operating at an EPD exhibits an enormous sensitivity to any perturbation to the system. In such a system, shown in Fig. 3, we have different EPD resonances for different modulation frequencies, hence we can design a sensor with exceptional sensitivity to operate at any of them. In order to illustrate the exotic performance of the described sensing system, we assume that the biosensing capacitor is experiencing a \(\delta\) increase in the concentration of the MUT, hence the biosensing capacitance value is perturbed as \(C_{bio}(\delta)\), and its relative change \(\delta C_{bio}\) follows the behavior shown in Figs. 4(c) and (d), for the two sensing scenarios shown in Fig. 3. In turn, a relative positive increment \(\delta C_{bio}\) perturbs the LTP-LC resonator operating at an EPD, generating two real resonance frequencies, whereas a negative \(\delta C_{bio}\) generates two resonance frequencies that deviate in their imaginary part, following the dispersion diagram in Fig. 3(b). These features are better shown in Fig. 6 that illustrates such ultra-sensitivity of the resonance frequency to small values of \(\delta C_{bio}\), considering three cases with three different modulation frequencies \(f_m\). Fig. 6(a) and (b) show the real and imaginary shifts of the resonance frequencies, respectively, where the solid-blue curve represents a design with a modulation frequency \(f_m = 112.6\) kHz, the dashed-red curve and green circles represent scaled designs of the biosensor with modulation frequencies \(f_m = 11.3\) MHz and \(f_m = 112.6\) MHz, respectively.

### V. Conclusion

We have exploited the concept of EPDs induced in linear time-periodic systems to achieve extremely sensitive biosensors based on the detection of a resonant frequency shift. We use a single time-varying LC resonator whose capacitance is given by the parallel arrangement of a time-variant capacitor and the biosensing capacitor. Furthermore, we have developed a model of interdigitated capacitors that well describes changes of capacitance due to the variations in the concentration of a MUT and investigated how sensitive is the LTP-LC biosensor to such changes. We have considered two different sensing scenarios, and an unprecedented sensitivity to the perturbations of the time-variant LC resonator at an EPD is illustrated. The sensitivity of the resonance frequency in a single, time-varying, LC resonator working at an EPD to perturbations has been demonstrated to be much higher than that of a single, time-invariant (i.e., standard), LC resonator. The practical implementation of this sensing technology seems straightforward since the time-modulated capacitance can be realized with a simple multiplier controlled by a modulated voltage pump \[45\] for example. The working principle for the proposed ultra-sensitive biosensor is general and can be easily implemented in existing systems to enhance sensitivity, paving the way to a new class of ultra-sensitive sensors.
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