Resonant slot antennas as transducers of DNA hybridization: A computational feasibility study

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***Abstract* — We propose and simulate a resonant slot antenna for sensing DNA hybridization. Using simple geometric arguments for water displacement from a DNA-functionalized surface, we predict the changes in dielectric constants caused by hybridization. We conclude that these changes are significant enough to be detected in measurements of the resonant frequency and the surface currents of a slot antenna. These results motivate experimental work using these antennas as alternatives to current fluorescence probes.**

I. Introduction

The study of DNA hybridization on surfaces is important to high-throughput sequencing, genetic screening and biomolecular sensing, yet conventional optical (fluorescence) techniques used to measure hybridization are difficult to integrate into sensors. Microwave probes offer a new alternative to fluorescence and can be fabricated using standard semiconductor techniques. Probes based on slot antennas [1], patch antennas [2-4], transmission line structures [5-8], and cavity resonators [9-10] have been used to study the dielectric properties of films and bulk materials. Fluid cells have been incorporated into transmission line structures to sense biomolecular solutions [11], and to observe surface chemistry involving aqueous-based macromolecules [12]. The extension of these microwave techniques to the study of surface chemistry is relatively new however, and there is a need for research using a well-understood process such as DNA hybridization to understand measurements made by these probes.

The resonant slot antenna is a simple probe that is well suited to the study of DNA hybridization. Its planar geometry permits its use in thin film measurements, and its symmetry permits its use in balanced measurements. In this paper, we demonstrate the feasibility of using the slot antenna for sensing DNA hybridization.

II. Dielectric Properties of DNA Hybridization

Various methods have been used to estimate the electrical properties of films and solutions with distinct constituents. McKee et. al. have investigated the dielectric constant of a mixture of two polar liquids with significantly different individual permittivities [13]. A number of other researchers have investigated the permittivities of aqueous solutions and interpereted their results in terms of a relaxation time for water in a hydration layer about the solute [14-16].

We choose a simple model for the dielectric constant of the DNA film in aqueous solution using the Wiener mixture equation [17]

$$\varepsilon_{eff} \le f_u \varepsilon_u + (1 - f_u)\varepsilon_v \qquad (1)$$

where f_u is the volume fraction of DNA molecules, ε_u is the dielectric constant of DNA, and ε_v is the dielectric constant of water ($\varepsilon_v = 64$). In our calculations, we take the loss tangent of water to be constant ($\tan\delta = 0.4$).

Upon hybridization, a complementary DNA strand from solution binds with a strand on the surface. To estimate the expected shift in dielectric constant of the DNA film due to hybridization, we assume that each double strand of hybridized DNA occupies a cylindrical volume with diameter 2 nm and length 0.34 nm per base pair. The hybridized strand sections contain 15 base pairs, for a total cylinder length of 5.1 nm, as illustrated in Fig. 1. Each cylindrical volume is $1.6\text{x}10^{-20}$ cm^3. The strands adhere to the surface with a density of $5\text{x}10^{12}$ molecules per cm^2. Thus, for a 1-cm^2 sample, the volume of water excluded from the DNA film upon hybridization is $8\text{x}10^{-8}$ cm^3.

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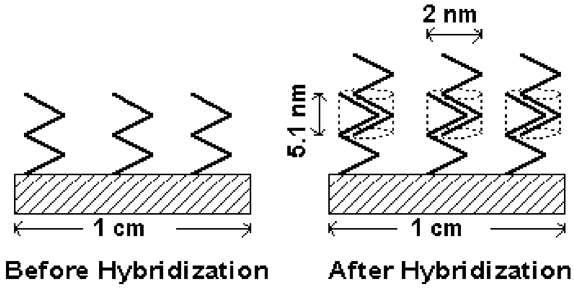

Fig. 1. Illustration of hybridized DNA geometry. The total volume of the sample, calculated by multiplying the cylinder height by the total sample area, is found to be 5.1x10^{-7} cm^3. Thus, after hybridization, $f_u \approx 0.1$.

The DNA film exhibits an increased conductivity along the molecular axis upon hybridization, causing an anisotropic dielectric constant [18]. The electric fields of the slot antenna, however, are oriented (largely) perpendicular to the strands. We assume that bulk DNA has a real-valued dielectric constant of $\varepsilon_r = 2$ normal to the axis. Thus, Equation 1 gives an upper-bound estimate of $\varepsilon_{eff} \leq 58$ for the effective dielectric constant of hybridized DNA.

A lower bound for the dielectric constant of the hybridized film can be calculated with another Wiener mixture equation. [15]:

$$\varepsilon_{eff} \geq \left(\frac{(1-f_u)}{\varepsilon_v} + \frac{f_u}{\varepsilon_u} \right)^{-1} \qquad (2)$$

Equation 2 gives $\varepsilon_{eff} \geq 15$ for the film after hybridization.

The volume fraction occupied by DNA before hybridization is unknown because even though all DNA strands have the same sequence of base pairs and are therefore nominally the same length, the individual molecules are highly flexible and can exhibit a wide range of conformations when tethered to the surface. As a first-order estimate, we assume that the unhybridized DNA volume fraction is negligible ($f_u \approx 0.0$). Consequently, the effective dielectric constant of the unhybridized DNA film is assumed to be $\varepsilon_{eff} = 64$.

The range of ε_{eff} for the hybridized DNA film, predicted by the Wiener equations, is then $15 \leq \varepsilon_{eff} \leq 58$. Comparing these values to the estimated effective dielectric constant of single-stranded (unhybridized) DNA ($\varepsilon_{eff} = 64$) suggests a 10% to 80% decrease in the dielectric constant as a result of hybridization.

III. Slot Geometry and Simulation

Our model of the slot antenna is constructed on a 0.81-mm-thick Rogers RO4003 substrate ($\varepsilon_r = 3.38$, $\tan\delta = 0.0027$) and fed from the back by microstrip as shown in Fig. 2. In an experimental setup, the DNA strands adhere to a surface immersed in a solution located on the metal side of the antenna.

The slot antenna transducer is simulated using a method of moments technique [19]. First, we investigate the case illustrated in Fig. 2a, where a homogeneous dielectric layer completely covers the antenna ground plane. The baseline dielectric constant of the layer is assumed to be that of the unhybridized DNA solution ($\varepsilon_r = 64$, $\tan\delta = 0.4$). The reflection coefficient (S_{11}) seen at the reference plane shown in Fig. 2a is calculated over a narrow band of frequencies around 9 GHz, the fourth slot resonance. Under these loading conditions, the matching between the source and the structure at the fourth resonance is better than that at the first, second, or third. The reflection coefficient of the slot is then tracked as the dielectric constant of this DNA solution is lowered due to hybridization by 1%, 5%, 10%, and 15%. (From the analysis presented in Section II, we expect at least a 10% change as a result of hybridization.) Fig. 3 shows the results of our simulation. The resonant frequency of the slot antenna increases monotonically with decreasing ε_{r2}. We note that resonant frequency shifts of this magnitude can be easily resolved using a network analyzer.

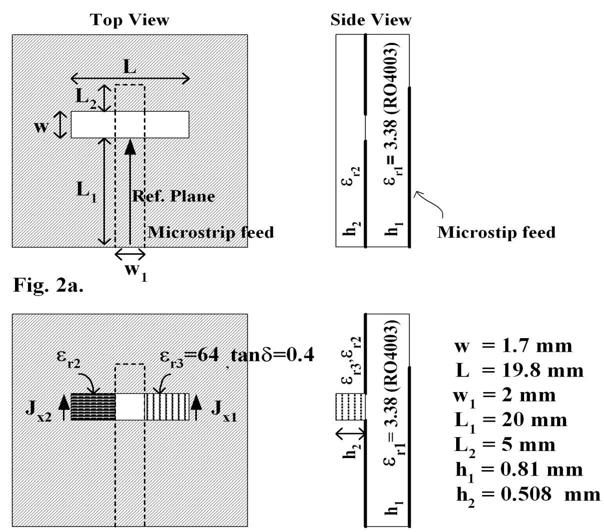

Fig. 2b.

Fig. 2. Balanced configuration for sensing hybridization.
a) Both sides of slot functionalized with identical DNA (ε_{r2}).
b) Each side of slot functionalized with different DNA so only one side (ε_{r2}) hybridizes in a test solution.

Second, we investigate the case illustrated in Fig. 2b, where the antenna is used as a balanced detector. Here, the antenna is loaded asymmetrically with dielectric bricks of different material properties. One brick contains unhybridized DNA solution (fixed dielectric constant, ε_{r3}) while the other contains DNA solution of a variable dielectric constant, ε_{r2}, the value of which depends on the state of hybridization. The goal is to observe the effects of this imbalance on the antenna's surface current distribution. The simulations for this geometry were performed using XFDTD [20]. As shown in Fig. 2b, the current density at the end of the slot on the control side is denoted as J_{x1}; the current density at the opposite end of the slot is denoted as J_{x2}.

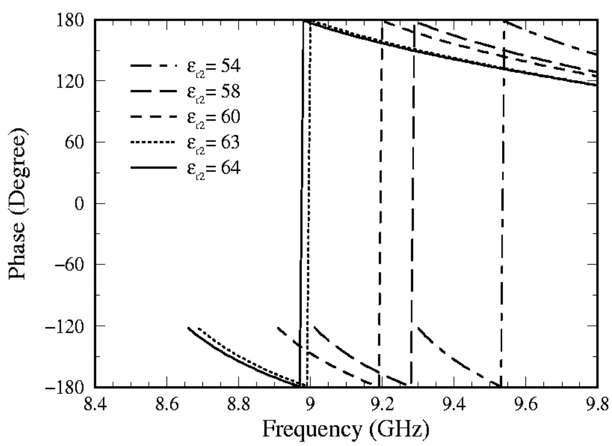

Fig. 3. Phase of reflection coefficient for 1%, 5%, 10%, and 15% changes in the dielectric constant of the DNA solution for the configuration shown in Fig. 2a.

Simulation results showing relatively large $|J_{x2} - J_{x1}|$ is shown in Fig. 4 for $\varepsilon_{r2} = 54$. Current densities shown are normalized to the (not shown) maximum current density seen at the first resonance. In Fig. 5, we plot the normalized current differences at three sample frequencies as a function of the fractional difference between the dielectric loading of each side of the slot. Current differences of this magnitude are easily observed with diode detectors and lock-in amplification. Therefore, it should be feasible to drive the antenna at a fixed frequency and sense the magnitude of $J_{x2} - J_{x1}$.

The solid-line and dotted-line curves in Fig. 4 show how the current densities on each side of the slot vary with frequency for a fixed dielectric imbalance ($\varepsilon_{r2} = 54$, $\varepsilon_{r3} = 64$). The frequency at which this sensor would work best is not immediately obvious from these curves. While the relationship between the current imbalance and the slot resonances is complicated and difficult to predict, a simple experiment could be done where the excitation frequency is swept after hybridization to determine the frequency of maximum sensitivity. Driving the slot at that frequency and observing the current difference in a second experiment could track the hybridization process in real time. We note that the DNA film can have a different sequence on either side of the slot so that hybridization will occur exclusively on one side. The symmetry of the slot antenna would then make the experiment insensitive to thermal drift and oscillator instabilities.

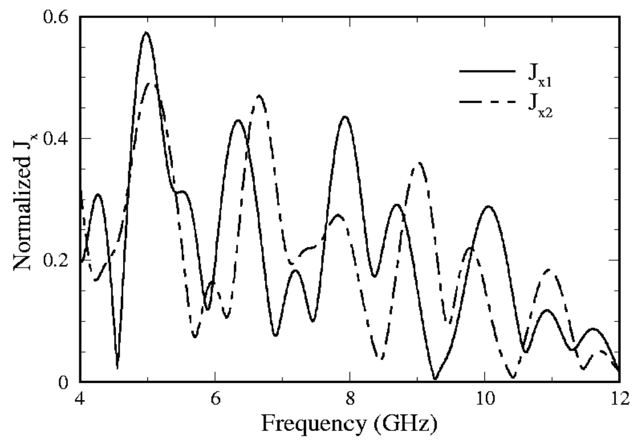

Fig. 4. Normalized surface current distribution resulting from asymmetric loading, ε_{r2} = 54 of the resonant slot. Current densities shown are normalized to the (not shown) maximum current density seen over the entire 1-15 GHz frequency range.

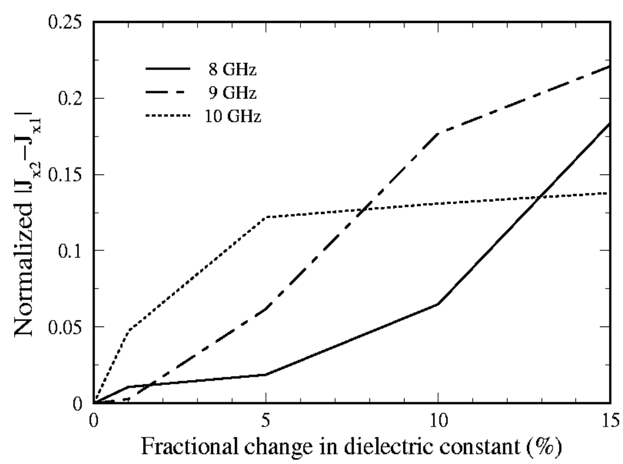

Fig. 5. Surface current differences, $|J_{x2} - J_{x1}|$ at 8, 9, and 10 GHz calculated with currents normalized as in Fig. 4.

IV. CONCLUSIONS

We have demonstrated the feasibility of using a resonant slot antenna as a sensitive transducer of DNA hybridization on a surface in solution. The sensitivity mechanism of the antenna can be either its resonant frequency or the imbalance of current on its surface.

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