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# A Linear, Time-Invariant Model for Cancerous and Normal Breast Tissue

M. Habibi, *Member, IEEE, and E. Diep*

*Abstract*— **Electrical properties of biological cells and human tissue have been used to characterize cancerous vs. normal tissue. Commonly, measured dielectric spectra (permittivity and conductivity) are fitted into an empirical function and the best-fit parameters of the function are considered as a tool to differentiate various types of tissue; however, these parameters do not provide any explanation for the underlying molecular structure. In this work, we modeled the frequency dependence of impedance data collected from human breast tissue using a high-order, linear, time-invariant filter. The results show that the parameters of the filter not only can be used to classify tissue types, they may provide meaningful information about the properties and structure of tissues.**

## I. Introduction

DIELECTRIC spectroscopy is a powerful tool for characterizing and classifying materials based on electrical properties. These properties are unique and directly related to the molecular structure of matter. An understanding of the dielectric properties of living cells, cellular aggregates, tissues, and organs has been of great interest since the beginning of the twentieth century [1]-[7]. It also has been discovered that the frequency dependence of dielectric spectra allows the identification and investigation of underlying mechanisms [8], [9].

Furthermore, dielectric spectroscopy has been used as a non-invasive tool to investigate the electrical properties of normal and cancerous human breast tissue [10],[11]. There are strong evidences that different types of human tissues have varying electrical properties [12], [13], however quantitatively interpreting the electrical data has been a challenge.

The raw dielectric data usually are collected in form of impedance (equivalent series of capacitance and resistance) or admittance (parallel connection of capacitance and conductance) over a range of frequencies. First, the data must be corrected for a number of residual errors, e.g. electrode polarization [13], [14]. Second, the data should be calibrated by applying a geometrical factor (or known as a cell constant). Finally, the results are fitted into an empirical function and the parameters of the function are used to characterize the tissue sample [10].

A number of empirical functions e.g. Debye, Cole-Cole [1], Cole-Davidson [15], and Universal Response [9], have been proposed for fitting the experimental data. These empirical functions have been employed to express dielectric spectra; yet the relationship between the function parameters and molecular/cellular structure of the sample under investigation has not been explained.

On the other hand, biological systems such as tissues can be approximated by linear, time-invariant (LTI) systems. The characteristics of these systems can be used to study the physical structure and properties of the system. Although, human tissue may not be a linear system, it can be modeled by high-order, LTI systems.

In this work, we investigated the LTI models of cancerous and normal human breast tissue. For modeling, we used the dielectric data which were collected from a number of patients in the radio frequency range (40Hz to 110MHz) and have been recently published. Since the data represent the frequency response of human breast tissue, it can be concluded that human tissue acts like a high-order analog filter.

We converted the data into a transfer function which represents an Infinite Impulse Response (IIR) filter, and then the filter is realized using direct-I form structure. Two transfer functions for normal and cancerous human breast tissue were obtained. It is also concluded that various filter parameters such as degree and location of poles/zeros can be used to differentiate cancerous and normal tissues. In addition, the filter parameters may have a potential to justify the physiological properties of human tissue.

## II. Methods

### A. Dielectric Spectra

The dielectric data analyzed in this work were recently collected and published [13]. The detail can be found in [13], but briefly, normal and cancerous breast tissues samples were acquired from a total number of 34 patients who underwent surgical mastectomy. These samples were diagnosed and characterized by a pathologist. The raw capacitance and conductance data for each frequency were converted into permittivity and conductivity spectra after applying the proper geometrical factor and correcting for electrode polarization effects. The spectra were then fitted to:

$$\varepsilon^* = \varepsilon_{hf} + \frac{\delta}{(j\frac{f}{f_0})^{\gamma} + (j\frac{f}{f_0})^{\beta}} - j\frac{\sigma_l}{2\pi\varepsilon_0 f} \qquad (1)$$

where $\varepsilon^*$ , $\varepsilon_{hf}$ , $\varepsilon_0$ are the complex permittivity, the high-frequency limit of permittivity, and the permittivity of free

M. Habibi is with the Minnesota State University, Mankato, Iron Range Engineering Program 55792 USA, (Tel: 218-404-6353; fax: 218-742-9169; e-mail: Mohammad.habibi@mnsu.edu)

E. Diep is with the Minnesota State University, Mankato, Iron Range Engineering Program 55792 USA (e-mail: Eric.diep@mnsu.edu).

 

space ($8.85\times10^{-12} Fm^{-1}$), respectively. $\sigma_l$ is the low frequency limit of conductivity; $f$ and $f_0$ are the frequency of applied field and the characteristic frequency; $\gamma,\beta,\delta$ are the function parameters. The properties of the biological system understudy were parameterized in terms of $f_0,\gamma,\beta,\delta,\varepsilon_{hf}$.

### B. Modeling the Dielectric Spectra Using a Transfer Function

In this work, we used these parameters ($f_0,\gamma,\beta,\delta,\varepsilon_{hf}$) as published in [13] and calculated the complex permittivity for each type of tissue (normal and cancerous) using equation (1). The admittance and impedance of the data were calculated using equations (2) and (3):

$$Y(\omega) = j\omega\varepsilon_0\varepsilon^* \tag{2}$$

and

$$Z(\omega) = \frac{1}{Y(\omega)} = \frac{1}{j\omega\varepsilon_0\varepsilon^*} \tag{3}$$

where $\omega = 2\pi f$ is the angular frequency. The next step is to model the impedance (or admittance) data by a transfer function. The transfer function is a convenient representation of a LTI system and is commonly used in the analysis of systems. Equation (4) describes a common form of a transfer function used in this work:

$$H(s) = \frac{s^m + a_1 s^{m-1} + ... + a_{m-1}s + a_m}{s^n + b_1 s^{n-1} + ... + b_{n-1}s + b_n} \tag{4}$$

where $s$ is the complex frequency, and $m$ , $n$ determine the degrees of numerator and denominator, respectively. By replacing $s$ with $j\omega$, equation (4) becomes:

$$H(j\omega) = H'(\omega) + jH''(\omega) \tag{5}.$$

$H'(\omega), H''(\omega)$ are the real and imaginary parts of the transfer function at each frequency. In order to find the system characteristics, the impedance data were fitted into equation (5), and then the fit was evaluated by the following residual function:

$$\mathrm{Re}\, s = \frac{\sum_{i=1}^{N}(Z'(\omega_i) - H'(\omega_i)) + \sum_{i=1}^{N}(Z''(\omega_i) - H''(\omega_i))}{N} \tag{6}$$

where $Z'(\omega)$ and $Z''(\omega)$ are the real and imaginary parts of the impedance data at each frequency, respectively. The best fit was determined by minimizing equation (6) for $m = 1,2,...,20.$ and $n = 1,2,...,20.$ The resulting parameters for the system include $m,n,a_1,...,a_m,b_1,...,b_n$.

## III. RESULTS AND DISCUSSION

### A. Accuracy of the Model

Using equation (6), the residual error was calculated for each structure by varying $m$ and $n$ from 1 to 20, i.e. $m = 1,2,...,20$ and $n = 1,2,...,20.$ Table I and Table II show a partial list of the residual error of the various structures for cancerous and normal tissue. Interestingly, the results reveal that only specific structure matches with the measured data. For instance, $m = 9$ and $n = 8$ produces the minimum residual error for cancerous tissue, and the pair $m = 8$ and $n = 7$ results in minimum error for normal tissue. Fig. 1 shows the magnitude and phase of the impedance data and the corresponding best-fit transfer function for both cancerous and normal breast tissue. It can be seen from Fig. 1 that the quality of the fit is excellent, suggesting that only specific structure matches with the data.

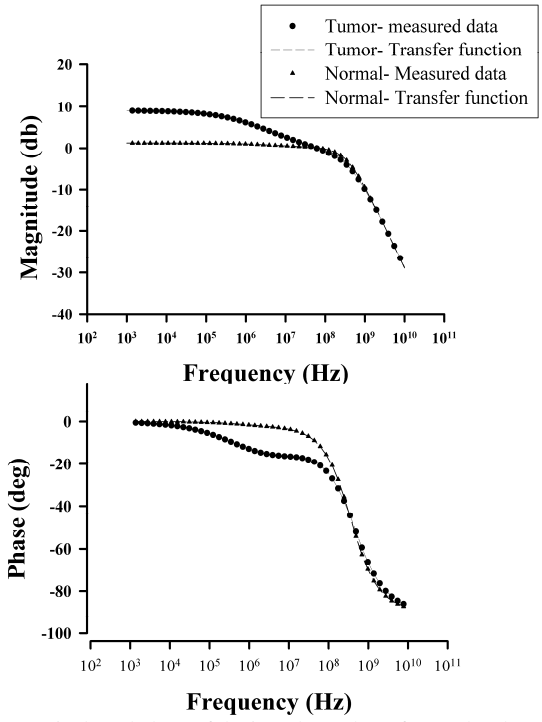


Fig. 1. Magnitude and phase of the impedance data of normal and cancerous tissue. The responses of corresponding transfer functions are shown by dashed lines.

TABLE I
RESIDUAL ERROR FOR CANCEROUS BREAST TISSUE

| | n=6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|
| m=6 | 0.1941 | 0.1861 | 0.1816 | 0.176 | 0.1725 |
| 7 | 0.1786 | 0.1729 | 0.1666 | 0.1632 | 0.1604 |
| 8 | 0.1494 | 0.0172 | 0.163 | 0.0398 | 0.2553 |
| 9 | 0.1567 | 0.1198 | **0.009** | 0.0889 | 0.2577 |
| 10 | 0.159 | 0.1429 | 0.159 | 0.1535 | 0.0412 |

Fig. 2 and Fig. 3 show the direct-I structures for both cancerous and normal breast tissue. Each structure consists of a set of integrators ($1/s$), a set of coefficients, and a differentiator $s$.

TABLE II
RESIDUAL ERROR FOR NORMAL BREAST TISSUE

| | n=6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|
| m=6 | 0.0112 | 0.0106 | 0.0102 | 0.0098 | 0.0094 |
| 7 | 0.0018 | 0.0096 | 0.0091 | 0.0092 | 0.0091 |
| 8 | 0.002 | **0.0004** | 0.0611 | 0.0913 | 0.0086 |
| 9 | 0.0032 | 0.0019 | 0.0016 | 0.1139 | 0.0268 |
| 10 | 0.0034 | 0.0927 | 0.1292 | 0.153 | 0.0808 |

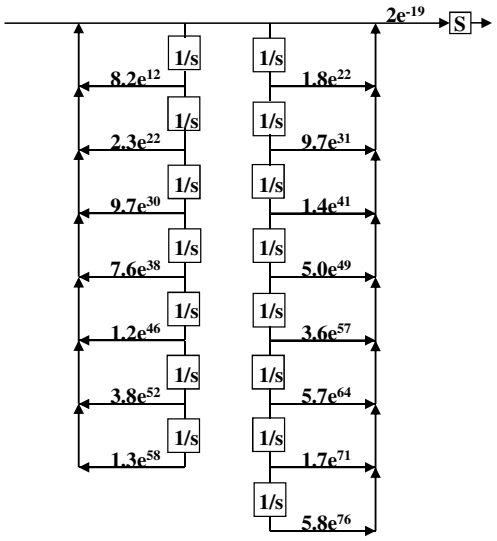


Fig. 2. Direct-I structure for normal breast tissue.

### B. Model Parameters

The impedance data were modeled by an LTI systems and a set of new parameters in time/frequency domains were produced and investigated. A few of these parameters such as gain margin (GM), phase margin (PM), crossover frequencies ($\omega_{cg}, \omega_{cp}$), poles, and zeros are shown in Table III and Table IV. The structure and coefficients, as shown in Fig. 2 and Fig. 3, can be used to extract the characteristic information of the model. These parameters are physically meaningful and can reveal important information about the system. For instance, the locations of poles/zeros provide information about the time response as well as the stability of the system. Phase margin and gain margin are measures of stability in systems. For example, phase margin determines relative stability, meaning the tendency of a system to oscillate when it is stimulated by an input signal; on the other hand, gain margin shows absolute stability which means the degree to which the system will oscillate without given any input. It is also an interesting observation that data were well-fitted in specific structures.

TABLE III
SYSTEM POLES AND ZEROS

| Cancerous Tissue | | Normal Tissue | |
|---|---|---|---|
| Poles | Zeros | Poles | Zeros |
| -1.82e5 | -1.70e5 | -3.9e5 | -3.94e5 |
| -1.96e6 | -1.64e6 | -3.44e6 | -3.37e6 |
| -1.27e7 | -9.30e6 | -1.66e7 | -1.60e7 |
| -6.8e7 | -4.98e7 | -7.62e7 | -7.35e7 |
| -3.61e8 | -2.81e8 | -3.92e8 | -3.78e8 |
| -2.02e9 | -1.42e9 | -2.36e9 | -1.90e9 |
| -1.96e10 | -3.42e9 | -8.15e-12 | -2.76e9 |
| **8.31e12** | -2.07e10 | | -1.87e22 |
| | -9.43e21 | | |

### C. Differentiating Tissue Type Using New Parameters

As shown in Table III, Table IV, Fig. 2, and Fig. 3, there are a number of parameters that vary based on the tissue type such as gain/phase margin, crossover frequencies, the location of poles/zeros, etc. As shown in Table III, the transfer function of cancerous tissue has a positive pole (on the right side of s-plane), which causes the system to become unstable. This parameter may be used to explain the properties of cancerous cells.

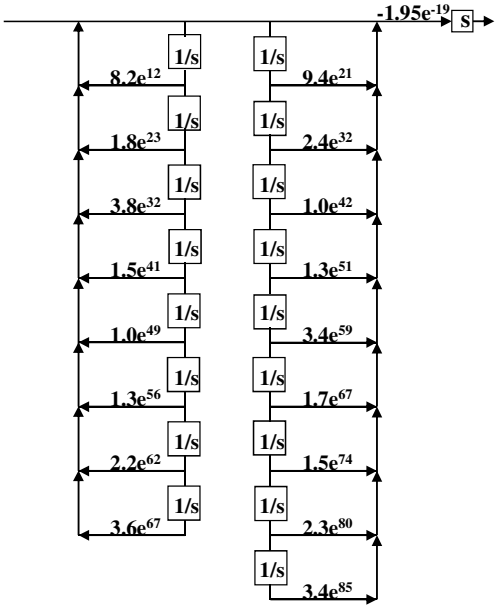


Fig. 3. Direct-I structure for cancerous breast tissue.

TABLE IV
SYSTEM PARAMETERS

| Tissue Type | GM | PM | $\omega_{cg}$ | $\omega_{cp}$ |
|---|---|---|---|---|
| Cancerous | 2.79e-4 | -159 | 2.8e17 | 3.73e8 |
| Normal | $\infty$ | -167 | - | 4.47e8 |

## IV. CONCLUSION

The electrical properties of living tissue vary according to the molecular structure of tissue. Traditionally, the dielectric spectra are fitted to an empirical function and the parameters of the function are used to characterize the tissue type. The previously published reports show that there are significant differences in the electrical properties of normal and diseased tissue; however they do not provide any meaningful concepts regarding the structure of underlying mechanisms. The dielectric spectra of human breast tissue indicate that human tissue is a nonlinear system, but it can be estimated by a high-order linear filter. In this work, we introduced a new method of modeling tissues based on using transfer functions. Two transfer functions, one for each type of tissue, were generated using impedance spectra and the parameters of these transfer functions were used to differentiate normal and cancerous tissue. The new parameters provide additional information about the tissue system that can be interpreted by control engineers. One question to be investigated is what the relationships are between the molecular structure and the parameters of the transfer function.

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