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A novel approach for parameter estimation of Fricke-Morse model using Differential Impedance Analysis

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Abstract. In this paper we presented a new approach for parameter estimation of Fricke-Morse model (2R-1C circuit) of biological cell. Proposed method is based on Differential Impedance Analysis and it was applied in parameter estimation of five electrical bioimpedances: Total Body Composition, Trunk-Trunk, Arm-Arm, Leg-Leg and Respiration Rate. The proposed method has been evaluated regarding the influence of the number of measurement frequencies on the overall numerical accuracy and processing time. Obtained results are compared with Complex Non Linear Least Squares data fitting and it was showed that presented approach is significantly faster (ratio of processing times depends on the number of measurement frequencies). Additional advantage of the proposed method is very low computation complexity (it is not iterative) so it can be easily implemented in portable and autonomous low-cost microcontroller-based systems for bioimpedance measurement and parameter estimation of the Fricke-Morse model in real-time.

Keywords. Bioimpedance, estimation, signal processing

1 Introduction

The electrical properties of biological tissues have been analyzed for many years. Even in early studies, it was recognized that analysis of electrical bioimpedance (EBI) can provide important information about tissue condition [1]. In 1925, Fricke and Morse presented their model of biological cell which consists of three elements (2R-1C circuit) as shown in Fig. 1 [2]. The impedance of a cell according to Fricke-Morse 2R-1C model, at some angular frequency, $\omega = 2\pi f$ [rad/s], is given with (1), where R_e presents the extracellular space, while the intracellular space and the membrane are presented as a series of resistor R_i and a capacitor C_m, respectively.

$$Z(\omega) = \frac{R_e(1 + j\omega R_i C_m)}{1 + j\omega(R_i + R_e)C_m} \quad (1)$$

In literature, many studies can be found in which parameter estimation of Fricke-Morse model was used as diagnosis tool. For example, examination of dielectric properties of meat [3], in vivo human lung tissue bioimpedance analysis [4], in vivo real-time myocardium tissue characterization [5], body water estimation [6], etc. Basically, if there is some change in tissue from normal condition, values of model parameters will change from values obtained when tissue was in normal condition.

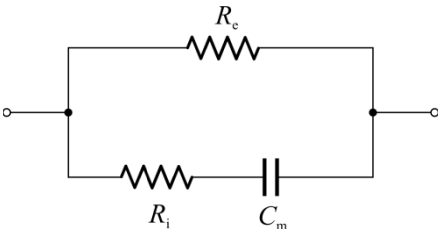

Fig. 1. Fricke-Morse model of biological cell.

However, some studies suggest use of more complex models which include fractional-order circuits [7] as they shown much better representation of experimentally obtained bioimpedance data. Complex models have been widely investigated in many fields of biology and biomedicine [8, 9], but they do not provide explanations related to the underlying structures and physical processes at the cellular level [10], thus Fricke-Morse model is used by many authors [11]. Moreover, parameter estimation of such models is usually based on complex non-linear least-squares (CNLS) method, based on the *Gauss–Newton* [12] or *Levenberg–Marquardt* [13] algorithms. The main disadvantages of such approach are [6, 13, 14]: (a) CNLS is time consuming process, (b) CNLS requires high quality initial guess for the model parameters, (c) there is always a possibility of converging into a local minimums, and (d) CNLS non-convergence is a common issue.

The differential impedance analysis (DIA) is a technique which can be used for parameter estimation as well as mod-

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el recognition [14-16]. The main advantage of non-iterative DIA approach is that it is not require initial guess for the model parameters. Moreover, DIA-based approaches for impedance analysis have been used in [5, 15, 16].

In this research, we analyzed use of DIA-based approach in parameter estimation of Fricke-Morse model. Our main consideration was to develop approach with low computation complexity suitable for portable and autonomous low-cost microcontroller-based systems for bioimpedance measurement and parameter estimation in real-time [17, 18].

2 A new approach for parameter estimation of Fricke-Morse model using Differential Impedance Analysis

In this study, a new method for real-time parameter estimation of the Fricke-Morse model with the use of only information about the real and imaginary parts of impedance ($\mathrm{Re}\{Z(\omega)\}$ and $\mathrm{Im}\{Z(\omega)\}$) at some angular frequency, ω [rad/s], together with the numerical calculated derivatives $\mathrm{dRe}\{Z(\omega)\}/\mathrm{d}\omega$ and $\mathrm{dIm}\{Z(\omega)\}/\mathrm{d}\omega$ is developed. The main purpose was to generate analytical expressions which can be used for direct computation of the parameters of the Fricke-Morse model without iterative process, which is the main characteristic of CNLS.

Real part of impedance of Fricke-Morse 2R-1C model (1) can be written as:

$$\mathrm{Re}\{Z(\omega)\} = K\frac{\omega^2 + zp}{\omega^2 + p^2} \tag{2}$$

and imaginary part as:

$$\mathrm{Im}\{Z(\omega)\} = K\frac{(p-z)\omega}{\omega^2 + p^2} \tag{3}$$

where K, z and p are defined as

$$K = \frac{R_e R_i}{R_e + R_i} \tag{4}$$

$$z = \frac{1}{C_m R_i} \tag{5}$$

$$p = \frac{1}{C_m (R_e + R_i)} \tag{6}$$

If we introduce $A(\omega)$, $B(\omega)$, $C(\omega)$ and $D(\omega)$ defined as:

$$A(\omega) = \frac{\mathrm{d}\,\mathrm{Re}\{Z(\omega)\}}{\mathrm{d}\omega} = \frac{2kp\omega(p-z)}{(\omega^2 + p^2)^2} \tag{7}$$

$$B(\omega) = \frac{\mathrm{d}\,\mathrm{Im}\{Z(\omega)\}}{\mathrm{d}\omega} = \frac{k(p-z)(p^2 - \omega^2)}{(\omega^2 + p^2)^2} \tag{8}$$

$$C(\omega) = \frac{\mathrm{Re}\{Z(\omega)\}}{\mathrm{Im}\{Z(\omega)\}} = \frac{\omega^2 + zp}{\omega(p-z)} \tag{9}$$

$$D(\omega) = \frac{\omega A(\omega)}{B(\omega)} = \frac{p^2 - \omega^2}{2p} \tag{10}$$

from the system of equations (2) and (9)-(10), parameters $p(\omega)$, $z(\omega)$ and $K(\omega)$ can be estimated with following equations:

$$p(\omega) = D(\omega) + \sqrt{D^2(\omega) + \omega^2} \tag{11}$$

$$z(\omega) = \frac{\omega(C(\omega)(D(\omega) + \sqrt{D^2(\omega) + \omega^2}) - \omega)}{\omega C(\omega) + (D(\omega) + \sqrt{D^2(\omega) + \omega^2})} \tag{12}$$

$$K(\omega) = \frac{\mathrm{Re}\{Z(\omega)\}(\omega^2 + (D(\omega) + \sqrt{D^2(\omega) + \omega^2})^2)}{\omega C(\omega) + (D(\omega) + \sqrt{D^2(\omega) + \omega^2})} \tag{13}$$

for each angular frequency ω.

By using these values, parameters of Fricke-Morse model can be calculated with following equations:

$$R_e(\omega) = \frac{z(\omega)K(\omega)}{p(\omega)} \tag{14}$$

$$R_i(\omega) = \frac{z(\omega)K(\omega)}{z(\omega) - p(\omega)} \tag{15}$$

$$C_m(\omega) = \frac{z(\omega) - p(\omega)}{z^2(\omega)K(\omega)} \tag{16}$$

for each angular frequency ω. Finally, estimated values R_e, R_i and C_m can be obtained as means of calculated values $R_e(\omega)$, $R_i(\omega)$ and $C_m(\omega)$, respectively.

The parameter estimation of the Fricke-Morse model with presented method at some angular frequency ω_i, i=1,2,..,N can be summarized with following five steps:

1. Measure the real and imaginary part of the impedance at ω_i, i=1,2,..,N, such that $\omega_1 < \omega_2 < ... < \omega_N$ (Re{$Z(\omega)$} and Im{$Z(\omega)$}), respectively.
2. Calculate the derivatives $d\mathrm{Re}\{Z(\omega_i)\}/d\omega_i$ and $d\mathrm{Im}\{Z(\omega_i)\}/d\omega_i$ at ω_i using impedance data from the nearest lower frequency point (ω_{i-1}).
3. Calculate the parameters $C(\omega_i)$ and $D(\omega_i)$ using (9) and (10).
4. Calculate the parameters $p(\omega_i)$, $z(\omega_i)$ and $K(\omega_i)$ using (11)-(13).
5. Calculate the parameters $R_e(\omega_i)$, $R_i(\omega_i)$ and $C_m(\omega_i)$ using (14)-(16) and assign these parameters to the frequency ω_i.

The distinguishing feature of the proposed method is that first estimated values are available after measurements at just two test frequencies.

Moreover, compared to the CNLS data fitting approach, advantages of proposed method are as well: (a) after first two measurements, new result is available after each new measurement, (b) shorter processing time because there is no need to simultaneously solve set of equations, (c) there is no possibility of converging into a local minimum or non-convergence because proposed method is not iterative, (d) the estimated solution (set of R_e, R_i and C_m) is unique which usually is not the case with CNLS data fitting, and (e) the presented algorithm has low computation complexity so it is expected that it can be used in portable and autonomous low-cost microcontroller-based systems for bioimpedance measurement and parameter estimation of the Fricke-Morse model in real-time.

One important consideration is that the accuracy of numerical differentiation highly depends on the quality of experimentally obtained impedance data and position of neighboring points. This points the possible implementation issues, as experimental bioimpedance data can be affected with noise, thus for implementation of systems for real-time bioimpedance measurement and parameter estimation of the Fricke-Morse model, signal filtering is unavoidable [11].

3 Evaluation of the proposed method

Proposed method has been evaluated regarding the influence of the number of measurement frequencies on the overall numerical accuracy and processing time. We analyzed parameter estimation of the Fricke-Morse model with proposed method of 5 common EBI-s: Total Body Composition (TBC), Respiration Rate (RR), Trunk-Trunk (TT), Leg-Leg (LL) and Arm-Arm (AA). Reference values for the model parameters (R_e, R_i and C_m) for each EBI are presented in Table 1 [18].

Table 1. Reference values for the model parameters [13]

EBI	R_e [Ω]	R_i [Ω]	C_m [nF]
TBC	917.50	629.00	3.42
RR	58.50	23.90	75.50
TT	99.00	42.30	44.00
LL	510.00	450.00	6.55
AA	364.60	379.00	6.20

Our proposed method has been compared with CNLS fitting regarding accuracy and processing time in frequency range of 10 kHz to 100 kHz, which is suitable for low-cost embedded bioimpedance measurement systems. CNLS data-fitting was performed in MATLAB® with *Levenberg-Marquardt* algorithm. Maximum number of function evaluations and maximum number of iterations were set to 10^3, while termination tolerance on the function value and termination tolerance on estimated vector were set to 10^{-9}. To increase the speed of estimation, a user-calculated Jacobian was supplied to the solver.

In Tables 2-4, calculated mean values and standard deviations of estimations with proposed DIA-based approach at six different number of measurement frequencies (N) are given for R_e, R_i and C_m, respectively. In the leftmost column, reference values for model parameter are given.

As it can be seen from Table 2, with increase of the number of frequency points in analyzed frequency range, mean values are closer to the reference value of the parameter and standard deviation is smaller. The same can be noticed for relative error, ΔR_e [%], made in estimation of R_e [Ω] when mean value of $R_e(\omega)$ [Ω] is assigned as estimated value. Moreover, it can be seen that with just 50 frequencies ΔR_e [%] is lower than 1 % for each EBI.

As it can be seen from Table 3, with increase of the number of frequency points in analyzed frequency range, mean values are closer to the reference value of the parameter and standard deviation is smaller. The same can be noticed for relative error, ΔR_i [%], made in estimation of R_i [Ω] when mean value of $R_i(\omega)$ [Ω] is assigned as estimated value. Moreover, it can be seen that in the most cases 500 frequencies is required to have ΔR_i [%] lower than 1 % for each EBI.

As it can be seen from Table 4, with increase of the number of frequency points in analyzed frequency range, mean values are closer to the reference value of the parameter and standard deviation is smaller. The same can be noticed for relative error, ΔC_m [%], made in estimation of C_m [nF] when mean value of C_m (ω) [nF] is assigned as estimated value. Moreover, it can be

Table 2. Mean values ± standard deviation of estimated values of R_e for different EBI-s.

R_e	N	ΔR_e [%]	R_e [Ω]±δR_e [Ω]
TBC R_e=917.50 Ω	10	3.651	951±0.17
	50	0.713	924.04±1.18
	100	0.355	920.76±0.59
	500	0.071	918.15±0.12
	1000	0.035	917.82±0.06
	5000	0.007	917.56±0.01
RR R_e=58.50 Ω	10	4.868	61.35±0.59
	50	0.949	59.06±0.12
	100	0.473	58.78±0.06
	500	0.094	58.56±0.01
	1000	0.047	58.53±0.01
	5000	0.009	58.51±0.00
TT R_e=99.00 Ω	10	4.795	103.75±0.98
	50	0.935	99.9±0.20
	100	0.466	99.46±0.10
	500	0.093	99.09±0.02
	1000	0.046	99.05±0.01
	5000	0.009	99.01±0.00
LL R_e=510.00 Ω	10	3.661	528.67±3.90
	50	0.714	513.64±0.82
	100	0.355	511.81±0.41
	500	0.071	510.36±0.08
	1000	0.035	510.18±0.04
	5000	0.007	510.04±0.01
AA R_e=364.60 Ω	10	2.730	374.55±1.79
	50	0.533	366.54±0.30
	100	0.266	365.57±0.15
	500	0.053	364.79±0.03
	1000	0.026	364.70±0.01
	5000	0.005	364.62±0.005

seen that in the most cases 100 frequencies is required to have ΔC_m [%] lower than 1 % for each EBI.

In these estimations CNLS approach generated results with relative errors lower than 0.005% for each EBI, independently of number of measurement frequencies. However, as it was explained before, proposed DIA-based approach has lower computation complexity because it is not iterative, thus it was expected that it has smaller processing time needed for parameter estimation. In Table 5, comparison of processing times required for CNLS and DIA approach is given. As it was expected, higher number of measurement frequencies requires more time for estimation for both approaches, but in

Table 3. Mean values ± standard deviation of estimated values of R_i for different EBI-s.

R_i	N	ΔR_i [%]	R_i [Ω]±δR_i [Ω]
TBC R_i=629.00 Ω	10	16.258	731.26±186.96
	50	2.412	644.17±27.26
	100	1.163	636.32±13.02
	500	0.226	630.42±2.51
	1000	0.113	629.71±1.25
	5000	0.022	629.14±0.25
RR R_i=23.90 Ω	10	21.292	28.99±9.40
	50	3.197	24.66±1.36
	100	1.543	24.27±0.65
	500	0.300	23.97±0.13
	1000	0.150	23.94±0.06
	5000	0.030	23.91±0.01
TT R_i =42.30 Ω	10	20.551	50.99±16.13
	50	3.082	43.60+2.34
	100	1.488	42.93+1.12
	500	0.289	42.42+0.22
	1000	0.144	42.36+0.11
	5000	0.029	42.31+0.02
LL R_i =450.00 Ω	10	10.872	498.93+106.57
	50	1.567	457.05+15.63
	100	0.752	453.38+7.47
	500	0.146	450.66+1.44
	1000	0.073	450.33+0.72
	5000	0.014	450.07+0.14
AA R_i =379.00 Ω	10	13.578	430.46+96.36
	50	1.991	386.54+13.71
	100	0.959	382.63+6.54
	500	0.186	379.71+1.26
	1000	0.093	379.35+0.63
	5000	0.019	379.07+0.13

all estimations DIA-based approach had significantly smaller processing times. It was faster 20-400 times.

Table 4. Mean values ± standard deviation of estimated values of C_m for different EBI-s.

C_m	N	ΔC_m [%]	C_m [nF] $\pm\delta C_m$ [nF]
TBC C_m=3.42 nF	10	5.336	3.60±0.0345
	50	0.987	3.45±0.006
	100	0.489	3.44±0.003
	500	0.097	3.42±0.001
	1000	0.049	3.42±0.0005
	5000	0.010	3.42±0.0005
RR C_m=75.70 nF	10	4.303	79.0±0.866
	50	0.785	76.3±0.137
	100	0.389	76.0±0.067
	500	0.077	75.8±0.013
	1000	0.038	75.7±0.007
	5000	0.008	75.7±0.001
TT C_m=44.00 nF	10	4.422	45.9±0.510
	50	0.809	44.4±0.082
	100	0.400	44.2±0.040
	500	0.079	44.0±0.007
	1000	0.040	44.0±0.004
	5000	0.008	44.0±0.001
LL C_m=6.55 nF	10	6.818	7.00±0.011
	50	1.270	6.63±0.019
	100	0.630	6.59±0.009
	500	0.125	6.56±0.002
	1000	0.063	6.55±0.001
	5000	0.012	6.55±0.000
AA C_m =6.20 nF	10	6.021	6.57±0.057
	50	1.120	6.27±0.011
	100	0.555	6.23±0.005
	500	0.110	6.21±0.001
	1000	0.055	6.20±0.0005
	5000	0.011	6.20±0.0005

Table 5. Comparison of processing times for DIA and CNLS approach.

	N	t_{DIA}[ms]	t_{CNLS}[ms]
TBC	10	0.024	8.819
	50	0.061	9.544
	100	0.123	7.592
	500	0.255	10.396
	1000	0.488	13.515
	5000	2.445	38.561
RR	10	0.015	7.576
	50	0.034	7.389
	100	0.103	6.553
	500	0.240	10.663
	1000	0.475	14.321
	5000	4.339	32.768
TT	10	0.020	5.167
	50	0.035	7.377
	100	0.057	7.495
	500	0.245	10.441
	1000	0.554	12.390
	5000	2.547	30.031
LL	10	0.023	5.583
	50	0.082	8.807
	100	0.189	8.874
	500	0.295	10.547
	1000	0.554	15.455
	5000	2.547	33.734
AA	10	0.019	5.454
	50	0.082	7.835
	100	0.112	5.419
	500	0.264	10.237
	1000	0.613	13.889
	5000	2.464	30.961

4 Conclusion

In summary, a new approach for parameter estimation of the Fricke-Morse model based on DIA is presented and it was shown that it can be used in real time impedance processing. The methodology presented in this work has been validated through simulations of electrical bioimpedance data obtained with 2R-1C circuit and reference values for model parameters taken from literature.

Although the proposed DIA-based approach cannot compete in accuracy with the CNLS, obtained accuracy is acceptable for many EBI applications, thus it can be used as alternative when the hardware resources are limited, e.g. low-cost microcontroller-based impedance measurement devices and when the computation time is reduced, e.g. for real time processing of time varying bioimpedance.

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