Investigation of the Applicability of Dielectric Relaxation Properties of Amino Acid Solutions Within the Resonant Recognition Model

Elena Pirogova*, George P. Simon, and Irena Cosic

***Abstract*—The resonant recognition model (RRM) is a physicomathematical approach used to analyze the interactions of a protein and its target, using digital signal processing methods. The RRM is based on the finding that there is a significant correlation between the spectra of numerical presentation of protein sequences and their biological activities. Initially, the electron–ion interaction potential was used to represent each amino acid in the protein sequences. In this paper, the dielectric constant (ε') and dielectric loss tangent ($\tan\delta$) parameters have been determined for their possible use in the RRM. These parameters are based on the values of capacitance and conductance obtained experimentally for 20 amino acid solutions using dielectric spectroscopy for the case of the real component of dielectric permittivity; the parameter used is the dielectric increment ($\Delta\varepsilon'$), the difference between dielectric constant of the amino acid solution and that of the solvent alone. The results of multiple cross-spectral analyses have shown that parameters analyzed generate in the consensus spectrum one dominant peak corresponding to the common biological activity of proteins studied, allowing the conclusion that these new parameters are suitable for use in the RRM approach.**

***Index Terms*—Amino acids, dielectric relaxation, digital signal processing, protein conductivity, protein function.**

I. Introduction

PROTEINS play a crucial role in almost every biological process, but are only able to express their biological function (interactions with their targets) when they achieve a certain active, native conformation, the so called three-dimensional (3-D) structure. Both protein function and its active 3-D structure are determined by the sequence of amino acids in the protein molecule. The novel physicomathematical approach called the resonant recognition model (RRM) [1], [2] is based on the transformation of the protein sequence into a numerical series by assigning to each amino acid in the sequence a physical parameter value relevant to the protein's biological activity. Previous investigations [4] have shown that parameters related to the energy of delocalized electrons of each amino acid are the most appropriate to use in the RRM. These findings can be explained by the fact that the electrons delocalized from the particular amino acid have the strongest impact on the electronic distribution of the whole protein. Initially, the energy of delocalized electrons [calculated from the general model of pseudopotentials [3] as the electron–ion interaction potential (EIIP)] of each amino acid residue was employed in the RRM approach [5]–[8]. In this study, to convert protein sequences into relevant numbers of parameters related to the protein's biological function, the dielectric permittivity properties of 20 amino acid solutions were measured. These newly measured parameter values have replaced the EIIP values, which were mathematically calculated from an approximate pseudopotential model [3]. The results obtained provide more accurate amino acid parameters, which lead to the improvement of active site predictions with the modified RRM.

Manuscript received March 3, 2003; revised March 17, 2003. *Asterisk indicates corresponding author.*

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Digital Object Identifier 10.1109/TNB.2003.813936

II. Methods

A. The Resonant Recognition Model

Biological processes in any living organism are based on selective interactions between particular biomolecules, in most cases proteins. The rules governing the coding of the protein's biological function, i.e., its ability to selectively interact with other molecules, have still not been elucidated. The RRM is an approach to identify the selectivity of protein interactions within the amino acid sequences. The RRM assumes that the specificities of protein interactions are based on the resonant electromagnetic energy transfer at the specific frequency for each interaction.

All proteins can be considered as a linear sequence of their constitutive elements, i.e., amino acids. The RRM interprets the protein linear information using signal analysis methods [1], [2]. It has been shown that certain periodicities (frequencies) within the distribution of energies of delocalized electrons along the protein are critical for protein biological function (i.e., interaction with its target). Once the RRM characteristic frequency for a particular biological function or interaction has been determined, it is possible to identify the individual amino acid's "hot spots," or domains that contribute most to the characteristic frequency and, thus, to the protein's biological function [1], [2].

The application of the RRM involves two stages of calculation. The first is the transformation of the amino acid sequence into a numerical sequence, each amino acid represented by the value of the electron–ion interaction potential (EIIP) [3], [4] describing the average energy states of all valence electrons in a

given amino acid. The EIIP values for each amino acid were calculated using the following general model of pseudopotentials [3]:

$$\langle \vec{k}+q|w|\vec{k}\rangle = \frac{0.25Z\sin(\pi 1.04Z)}{(2\pi)} \quad (1)$$

where q is a change of momentum of the delocalized electron in the interaction with potential w, while

$$Z = \frac{(\Sigma Z_i)}{N} \quad (2)$$

where Z_i is the number of valence electrons of the ith component of each amino acid, and N is the total number of atoms in the amino acid. A unique number can, thus, represent each amino acid or nucleotide, irrespective of its position in a sequence. Numerical series obtained this way are then analyzed by digital signal analysis methods in order to extract information pertinent to the biological function. The original numerical sequence is transformed to the frequency domain using the discrete Fourier transform (DFT). As the average distance between amino acid residues in a polypeptide chain is about 3.8 Å, it can be assumed that the points in the numerical sequence derived are equidistant. For further numerical analysis, the distance between points in these numerical sequences is set at an arbitrary value $d = 1$. Then, the maximum frequency in the spectrum is $F = 1/2d = 0.5$. The total number of points in the sequence influences the resolution of the spectrum only. Thus, for N-point sequence the resolution in the spectrum is equal to $1/N$. The nth point in the spectral function corresponds to the frequency $f = n/N$. In order to extract common spectral characteristics of sequences having the same or similar biological function, the following cross-spectral function was used:

$$S_n = X_n Y_n^* \quad n = 1, 2, \ldots, \frac{N}{2} \quad (3)$$

where X_n are the DFT coefficients of the series $x(m)$, and Y_n^* are complex conjugate DFT coefficients of the series $y(m)$. Peak frequencies in the amplitude cross-spectral function define common frequency components of the two sequences analyzed. To determine the common frequency components for a group of protein sequences, the absolute values of multiple cross-spectral function coefficients M have been calculated as follows:

$$|M_n| = |X1_n| \cdot |X2_n| \cdots |XM_n|, \quad n = 1, 2, \ldots, \frac{N}{2}. \quad (4)$$

Peak frequencies in such a multiple cross-spectral function denote common frequency components for all sequences analyzed. Signal-to-noise ratio (S/N) for each peak is defined as a measure of similarity between sequences analyzed. S/N is calculated as the ratio between signal intensity at the particular peak frequency and the mean value of the whole spectrum. The extensive experience gained from previous research [1], [2] suggests that a S/N of at least 20 can be considered as significant. The multiple cross-spectral function for a large group of sequences with the same biological function has been named the consensus spectrum. The presence of a peak frequency with significant S/N in a consensus spectrum implies that all of the analyzed sequences within the group have one frequency component in common. This frequency is related to the biological function provided the following criteria are met:

1) Only one peak exists for a group of protein sequences sharing the same biological function.
2) No significant peak exists for biologically unrelated protein sequences.
3) Peak frequencies are different for different biological functions.

In our previous studies, these criteria have been tested with over 1000 proteins from 25 functional groups [1], [2]. The following fundamental conclusion was drawn from our studies: *each specific biological function of protein or regulatory DNA sequence(s) is characterized by a single frequency*. Once the characteristic frequency for a particular protein function (interaction) is identified, it is then possible to utilize the RRM approach to predict the amino acids in the sequence that predominantly contribute to this frequency and are crucial for the observed function [5]. Finally, it is possible to design peptides having the desired periodicities [6]. Such peptides have been shown to express the desired biological function; examples shown in preliminary work include FGF peptidic antagonists [7] and HIV envelope agonists [8].

The RRM is based on the finding that distribution of delocalized electron energies along the protein molecule plays a crucial role in determining the protein biological activity [1], [2]. Indeed, it has been found that proteins having the same biological function (same target or receptor) share the same periodicities (frequencies) in this energy distribution. These frequencies are characteristics of a particular biological process. Although receptors share the same characteristic frequency with ligand proteins, which indicates that their recognition is on the basis of periodic matching between energy distributions, the phase at particular frequency is opposite (phase shift close to $\pm\pi = \pm 3.14$ rad between receptors and ligands) [1], [2].

B. Dielectric and Conductive Properties of Amino Acids

Amino acids are the basic structural units from which proteins are formed. Depending on the pH of the local environment, amino acids can take a number of different ionized states: acid form, neutral form, and base form. Each amino acid possesses a different side-chain, and these can be small or quite large, and also has a particular charge distribution.

As mentioned previously, the selectivity of protein interactions within the amino acid sequence could be identified if appropriate physical parameters are used [1], [2]. With the continuing aim to facilitate and improve the current RRM approach, measurements of dielectric permittivity have been undertaken to probe and quantify the physical differences for different amino acids.

C. Technique

For more than 40 years, experimental dielectric bridge methods have been employed in some form for low molecular mass materials and polymers [9], [10], but almost no work has been performed on amino acids. Although there are a number of different bridge configurations, the basic principle of operation is largely the same, and involves the balancing of the impedance of the two opposite arm pairs of the bridge.

One of these arms contains the sample, which may be modeled as a resistor R_s in parallel with a capacitor C_s. The technique [11]–[13] proposed in this paper is designed to measure values of the sample capacitance (C_p, F) and conductance (G, S) over a frequency range of 20 Hz to 10 MHz, in which a sinusoidal voltage is applied and the resulting current phase and amplitude determined. The main variables we are interested in measuring are C_p sample capacitance (μF), G sample conductance (μS), which are required to calculate ε' (sample dielectric constant), and $\tan\delta$ (sample loss tangent). Dielectric constant and capacitance relate to a material's ability to store charge, and conductance (and loss) to dipole and/or charge motion. During the experiment, we measured the values of the capacitance and conductance of 20 amino acid solutions from which the parameters described later can be determined.

In general terms, to determine dielectric properties of solids, a film is produced and its capacitance C_p and conductance G measured between two conducting parallel plates as a function of frequency, with the dielectric constant and dielectric loss being defined by

$$\varepsilon' = \frac{C_p}{C_o} \tag{5}$$

$$\varepsilon'' = \frac{\frac{G}{\omega}}{C_o}. \tag{6}$$

In this case C_o is the empty capacitance, the capacitance of the empty cell, with the thickness being the same as the sample, and is given by

$$C_o = \frac{\varepsilon_o A}{d} \tag{7}$$

where d and A are the sample area and thickness, respectively, and ε_o is the permittivity of free space. However, to measure the properties of amino acid solutions, a different electrode was used in this work—interdigitated comb electrodes, in which the electrode are patterned onto an inert substrate (usually polymer) surface. They work by fringing field measurements, in which the electric field "jumps" between adjacent combs the depth of the sample sensed is similar to the electrode spacing. These are readily placed into an amino acid solution and can be used over a wide frequency range. These sensors are often used for the following cure, such as ion mobility and dipole strength, in epoxy resins [14]. Using this electrode, measurement of capacitance and conductance could readily be made of the electrode alone, of the solvent (water or acid solution), or the polymer solution.

D. Sample Preparation and Experimental Measurements

All amino acids are white crystalline solids, which melt at high temperatures ($> 200\ ^\circ$C), some with decomposition. They are soluble in water but they vary considerably in their solubility. Furthermore, the solubility of any acid increase as the solution is made basic or acidic, being insoluble in organic solvents. These properties are a direct consequence of the dual basic–acidic character of amino acids which gives rise to ionic behavior. Based on different physicochemical properties of analyzed amino acids, we have used distilled water and 1-M HCL as a solvent environment for preparation of sample solutions.

Alanine, arginine, glycine, lysine, proline, serine, threonine, valine, and cysteine amino acids were dissolved in distilled water at room temperature using the magnetic stirrer. These amino acids were easily completely dissolved, obtaining clear solutions. Asparagine and histidine were dissolved in water using a hot plate magnetic stirrer, obtaining clear and light-yellow solutions, respectively. Methionine, glutamine, and tryptophan were dissolved in water using the sonocation technique [15], obtaining clear solutions. Leucine, isoleucine, aspartic acid, glutamic acid, phenylalanine, and tyrosine were dissolved completely in 1-M HCL at room temperature using the magnetic stirrer, obtaining clear solutions.

To run dielectric measurements, we prepared aqueous solutions of 0.5 M concentration of the following amino acids: alanine, arginine, glycine, lysine, proline, serine, threonine, valine, cysteine, asparagine, histidine, methionine, glutamine, and tryptophan. HCL solutions of leucine, isoleucine, aspartic acid, glutamic acid, phenylalanine, and tyrosine were also prepared. The experimental measurements of capacitance and conductance of our samples (amino acid solution, 60 ml) have been undertaken using HP4284 RLC Bridge (20 Hz to 10 MHz) [11], [12] and Software Win DETA V3.71. The liquid cell used in these measurements consists of the glass container with a Micromet (Munich, Germany) interdigitated electrode (IDEX A/D # 80) attached [13]. The experimental values such as capacitance and conductance are given in Table I-A and I-B.

E. Identification of the RRM Characteristic Frequencies Using the New Measured Dielectric Constant of Amino Acids Parameter

After completing the experimental measurements of capacitance and conductance of amino acid solutions, the experimental values of dielectric parameters, dielectric constant difference ($\Delta\varepsilon'$), and dielectric loss ($\tan\delta$) were calculated as follows.

1) Calculation of ε' of the sample (amino acid in solvent), where C_o is capacitance of the interdigitated electrode in air:

$$\varepsilon'_{\text{sample}} = \frac{C_{\text{psample}}}{C_o}. \tag{8}$$

2) Calculation of ε' of distilled water and ε' of HCL, respectively:

$$\varepsilon'_{\text{water}} = \frac{C_{\text{pwater}}}{C_o} \tag{9}$$

$$\varepsilon'_{\text{HCL}} = \frac{C_{\text{pHCL}}}{C_o}. \tag{10}$$

3) Calculation of the dielectric constant increment $\Delta\varepsilon'$ for amino acid aqueous solutions:

$$\Delta\varepsilon'_{\text{amino acid}} = \varepsilon'_{\text{sample}} - \varepsilon'_{\text{water}}. \tag{11}$$

4) Calculation of the dielectric constant increment $\Delta\varepsilon'$ for HCL amino acid solutions:

$$\Delta\varepsilon'_{\text{amino acid}} = \varepsilon'_{\text{sample}} - \varepsilon'_{\text{HCL}}. \tag{12}$$

5) Calculation of $\tan\delta$ of the sample:

$$\tan\delta = \frac{\varepsilon''}{\varepsilon'} = \frac{\left(\frac{G_{\text{sample}}}{\omega}\right)}{C_{\text{psample}}} \tag{13}$$

TABLE I

A. CAPACITANCE (μF), CONDUCTANCE (μS), DIELECTRIC CONSTANT (ε') AND DIELECTRIC LOSS TANGENT ($\tan\delta$) OF AMINO ACID AQUEOUS SOLUTION. B. CAPACITANCE (μF), CONDUCTANCE (MS), DIELECTRIC CONSTANT (ε') ND DIELECTRIC LOSS TANGENT ($\tan\delta$) OF AMINO ACIDS DISSOLVED IN HCL

Amino	Sample 1		Sample 2		Sample 3		Sample 4		Average Value		STD	
Acid	Cp	G	Cp	G	Cp	G	Cp	G	Cp	G	Cp	G
Alanine	2.277	303.11	1.878	272.24	1.863	274.47	1.993	280.51	2.003	282.58	0.1918	14.124
Arginine	11.82	433.50	12.27	447.61	12.43	456.91	12.58	460.78	12.28	449.70	0.3287	12.132
Asparagine	4.984	312.35	5.085	324.89	4.964	325.39	4.868	323.55	4.975	321.55	0.0890	6.179
Cysteine	3.970	399.48	3.956	410.53	3.917	415.70	3.876	418.61	3.930	411.08	0.0423	8.424
Glycine	3.362	287.47	3.418	297.07	3.512	301.55	3.503	305.59	3.449	297.92	0.0717	7.787
Histidine	6.204	279.51	6.530	315.68	6.357	324.16	6.015	323.27	6.277	310.66	0.2194	21.110
Lysine	8.986	304.32	9.339	320.33	9.401	325.35	9.470	327.87	9.299	319.47	0.2154	10.573
Proline	2.064	273.88	2.103	272.06	2.056	267.99	1.914	262.36	2.034	269.07	0.0828	5.108
Serine	2.082	223.83	2.160	239.55	2.193	243.90	2.214	247.53	2.162	238.70	0.0580	10.438
Threonine	2.165	267.26	2.278	288.95	2.279	290.78	2.292	292.75	2.254	284.94	0.0593	11.885
Valine	2.740	243.87	2.695	252.46	2.670	253.40	2.654	252.80	2.690	250.63	0.0375	4.525
Glutamine	6.467	317.79	5.994	301.06	5.858	293.23	5.738	276.65	6.014	297.18	0.3194	17.097
Methionine	4.756	406.81	4.829	415.21	4.380	395.31	3.306	349.60	4.318	391.73	0.7026	29.249
Tryptophan	2.179	219.40	2.143	215.97	2.148	213.78	2.118	211.24	2.147	215.10	0.0250	3.459

Table I-A

Cp sample/ Cp H2O	G sample/ G H2O	ε'x10^6 sample	$\Delta\varepsilon'$x10^6 amino acid	tan δ sample
3.882	2.277	0.0741	0.0550	22.465
23.798	3.624	0.4542	0.4351	5.8313
9.641	2.591	0.1841	0.1650	10.290
7.616	3.313	0.1457	0.1266	16.656
6.684	2.401	0.1276	0.1085	13.755
12.165	2.503	0.2322	0.2131	7.881
18.021	2.574	0.3440	0.3249	5.4706
3.942	2.168	0.0752	0.0561	21.065
4.190	1.923	0.0710	0.0519	17.581
3.602	2.296	0.0834	0.0643	20.130
5.213	2.020	0.0995	0.0804	14.836
11.655	2.395	0.2225	0.2034	7.869
8.368	3.157	0.1597	0.1406	14.446
11.161	1.733	0.0794	0.0603	15.953

Table I-A (*continued.*)

Amino	Sample 1		Sample 2		Sample 3		Sample 4		Average Value		STD	
Acid	Cp	G	Cp	G	Cp	G	Cp	G	Cp	G	Cp	G
Glutamic Acid	104.41	13.019	103.43	13.054	99.083	12.881	94.884	12.913	100.45	12.967	4.3746	0.0814
Tyrosine	81.298	14.453	82.702	15.246	86.057	14.683	88.878	14.076	84.734	14.615	3.4087	0.4897
Leucine	96.733	14.112	92.622	12.915	90.997	12.313	91.805	11.751	93.039	12.773	2.5503	1.0115
Isoleucine	84.423	14.753	81.422	12.734	84.525	11.764	86.713	11.202	84.271	12.568	2.1732	1.5606
Phenylalanine	97.267	9.282	95.934	9.164	95.687	9.109	96.519	9.094	96.352	9.162	0.7029	0.0853
Aspartic Acid	87.188	10.131	96.321	9.563	103.85	9.435	107.77	9.497	98.782	9.657	9.0728	0.3206

Table I-B

Cp sample/ Cp HCL	Gsample G HCL	ε'x10^6 sample	$\Delta\varepsilon'$x10^6 amino acid	tan δ sample
1.2425	0.8259	3.7156	0.7251	20.555
1.0481	0.9308	3.1342	0.1437	27.465
1.1508	0.8135	3.4114	0.4209	21.861
1.0423	0.8005	3.1171	0.1266	23.748
1.1918	0.5835	3.5640	0.5735	15.142
1.2218	0.6151	3.6539	0.6634	15.567

Distilled water:	**Cp**=0.516 μF	**G**=124.097 μS	ε'=0.0191x10^6
HCL:	**Cp**=80.848 μF	**G**=15.701 mS	ε'=2.9905x10^6
Empty cell:	**Co**=27.035 pF	**G**=0.00034 μS	

Table I-B (*continued.*)

where ω is an angular frequency in radians, $\omega = 2\pi f$,where f is in hertz. This determination of $\Delta\varepsilon'$ in particular has been reported elsewhere [16] as a useful method for obtaining a measure of the polarity of the dissolved polymer, dependent on concentration, as well as its chemical properties, chain–solvent and chain–chain interactions.

TABLE II
EIIP, $\Delta\varepsilon'$, AND $\tan\delta$ PARAMETER VALUES AND THEIR CORRELATION COEFFICIENTS

Amino Acid	EIIP	$\Delta\varepsilon'_{\text{amino acid}}$	$\tan\delta_{\text{sample}}$
L	0.0000	0.4209	21.861
I	0.0000	0.1266	23.748
N	0.0036	0.1650	10.290
G	0.0050	0.1085	13.755
V	0.0057	0.0804	14.836
E	0.0058	0.7251	20.555
P	0.0198	0.0561	21.065
H	0.0242	0.2131	7.881
K	0.0371	0.3249	5.471
A	0.0373	0.0550	22.465
Y	0.0516	0.1437	27.465
W	0.0548	0.0603	15.953
Q	0.0761	0.2034	7.869
M	0.0823	0.1406	14.446
S	0.0829	0.0519	17.581
C	0.0829	0.1266	16.656
T	0.0941	0.0643	20.130
F	0.0946	0.5735	15.142
R	0.0959	0.4351	5.831
D	0.1263	0.6634	15.567
R cor. coef. EIIP		0.1984	-0.1871

TABLE III
PEAK FREQUENCY AND SIGNAL-TO-NOISE RATIO VALUES FOR PROTEIN GROUPS

Protein Group	$\Delta\varepsilon'_{\text{amino acid}}$		$\tan\delta_{\text{sample}}$	
	f	S/N	f	S/N
Glucagon	0.3359	183.0	0.3789	205.8
Lysozyme	0.0645	197.5	0.2520	250.6
FGF	0.1055	147.4	0.0781	211.6
Cytochrome C	0.2773	227.3	0.0645	195.5
EGF	0.1230	102.4	0.4727	241.7
Myoglobin	0.3066	253.0	0.0586	255.1

III. RESULTS

The experimental measurements of conductance and capacitance of prepared amino acid solutions were performed; the values are given in Table I-A and I-B. The values of the dielectric constant and dielectric loss tangent parameters have been calculated and are presented in Table II. In this study, the RRM was employed for the structure–function analysis (determination of the characteristic profiles) of different protein groups. Glucagon, lysozyme, FGF, cytochrome C, EGF, and myoglobin were investigated and results compared using the EIIP, $\Delta\varepsilon'_{\text{amino acid}}$, and $\tan\delta$ parameters.

To determine the characteristic frequencies of analyzed proteins, a multiple cross-spectral analysis was performed for each protein group using the selected parameter values. The peak frequency and S/N values for each analyzed protein group were obtained, and are shown in Table III. For example, the multiple cross-spectral functions of Glucagon using the corresponding values of comparable EIIP, $\Delta\varepsilon'_{\text{amino acid}}$, and $\tan\delta$ parameters are presented in Figs. 1–3.

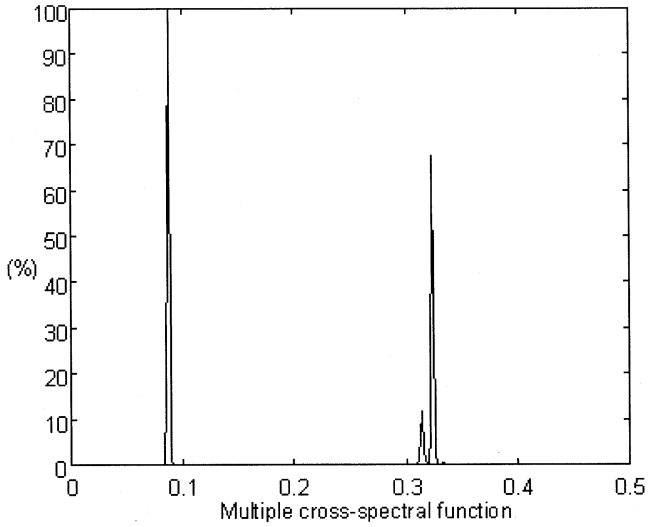

Fig. 1. Multiple cross-spectral function of Glucagon using the EIIP parameter.

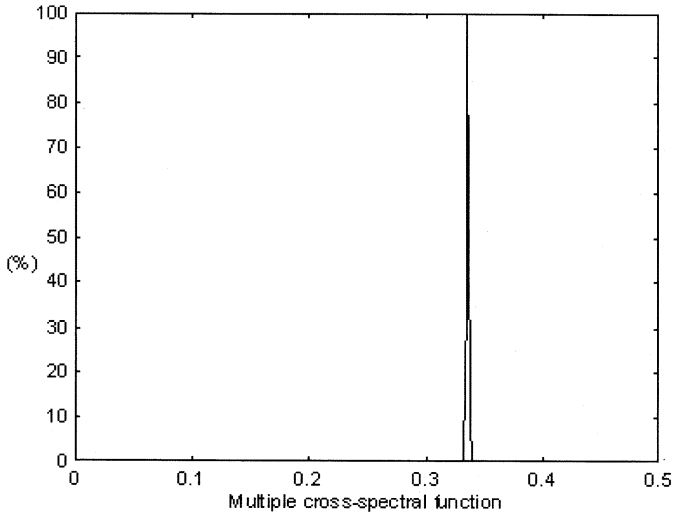

Fig. 2. Multiple cross-spectral function of Glucagon using $\Delta\varepsilon'_{\text{amino acid}}$ parameter.

Results of the RRM analysis of glucagon, lysozyme, FGF, cytochrome C, EGF, and myoglobin proteins indicate the RRM frequencies obtained are different for all analyzed protein groups using the EIIP, $\Delta\varepsilon'_{\text{amino acid}}$, and $\tan\delta$ parameters (see Table III). This is expected, as comparable parameters are not significantly correlated. The correlation coefficient between the EIIP and the $\Delta\varepsilon'_{\text{amino acid}}$ is 0.1984, and the correlation coefficient between the EIIP and the $\tan\delta$ parameters is -0.1871 (see Table II). However, the $\Delta\varepsilon'_{\text{amino acid}}$ and $\tan\delta$ parameters generate only one prominent peak in the consensus spectra of glucagon, lysozyme, hemoglobin, cytochrome C, and myoglobin proteins.

This corresponds to the idea that all the analyzed sequences within the protein group share the same biological function (satisfaction of the RRM criteria A), reinforcing the concept that this frequency determined by the RRM is characteristic of the specific biological function of studied proteins.

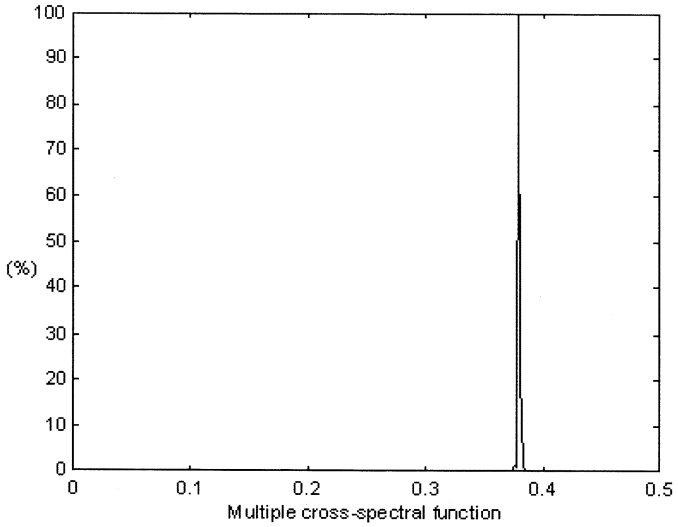

Fig. 3. Multiple cross-spectral function of Glucagon using $\tan\delta$ parameter.

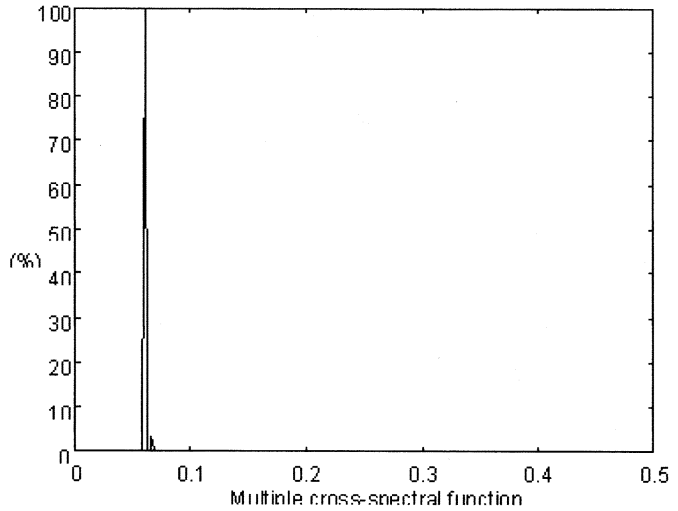

Fig. 4. Multiple cross-spectral function of EGF using the EIIP parameter.

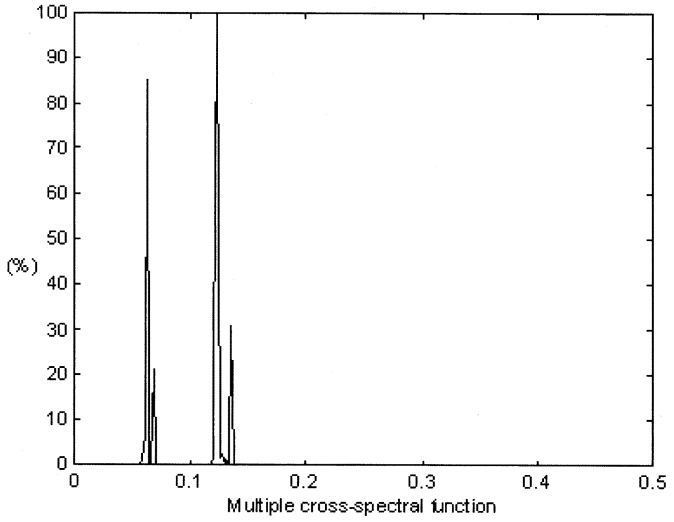

Fig. 5. Multiple cross-spectral function of EGF using $\Delta\varepsilon'_{\text{amino acid}}$.

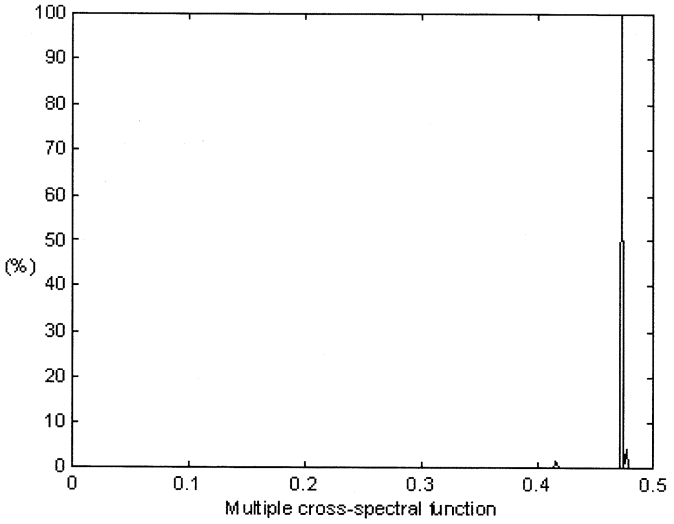

Fig. 6. Multiple cross-spectral function of EGF using $\tan\delta$ parameter.

It has been previously shown [1], [2] that a strong correlation exists between the amplitude spectrum of the numerical presentation of sequences and the corresponding biological function, essentially recognition between participants in a biological process. This model assumes that one protein can participate in more than one biological process; i.e., it may have more that one biological function, but that each RRM frequency characterizes a single biological function.

It is interesting to note that for EGF protein group (see Figs. 4–6), we observe different prominent peaks (different characteristic frequencies) at $f = 0.0620$, $f = 0.1230$, and $f = 0.4727$, identified using the EIIP, $\Delta\varepsilon'_{\text{amino acid}}$, and $\tan\delta$ parameters, respectively. As mentioned, each specific biological function is characterized by a single frequency. In our previous work [1], we reported that $f = 0.0620$ determined for EGF proteins using the EIIP parameter [2] represents biological information for EGF-specific receptor activation. Moreover, from Fig. 5, we observe three different characteristic frequencies using the $\Delta\varepsilon'_{\text{amino acid}}$ indicative of three different biological functions identified for EGF proteins. It is also important that among these three frequencies detected by the $\Delta\varepsilon'_{\text{amino acid}}$ parameter (see Fig. 5), one ($f = 0.0620$) is the same as detected by the EIIP parameter (see Fig. 4), although the frequencies have different amplitude ratios. This difference in the amplitude ratio values indicates why different frequencies were determined using the EIIP and $\Delta\varepsilon'_{\text{amino acid}}$ parameters.

IV. Discussion and Conclusion

The comparable analysis of the use of newly introduced amino acid solution properties, the dielectric constant and dielectric loss tangent, for structure–function predictions of biological profiles of different proteins within the RRM has been performed.

It should be noted that this analysis is subject to the following limitation: the measurements of experimental values of capacitance and conductance of amino acid solutions have been undertaken using two different solvents, distilled water and HCL, for the preparation of analyzed solutions. It is recommended for future work to design the measurements using the same solvent environment for all 20 analyzed amino acids; for instance, we

can use HCL or prepare less concentrated aqueous solutions of analyzed amino acids (< 0.5 M). According to the results presented and following the aim of the analysis of the possible use of the $\Delta\varepsilon'_{\text{amino acid}}$ and $\tan\delta$ parameters for structure–function predictions within the RRM, we conclude that these parameters could be suitable for the determination of characteristic profiles of studied proteins. The parameters allow us to detect the particular RRM frequency characteristic of the specific biological function of the protein studied, while satisfying the required RRM criteria. However, the further analysis of other protein families as well as the "hot spots" analysis and the peptides' design within the RRM would be needed to validate the suitability of the dielectric constant and loss parameters in a more general sense.

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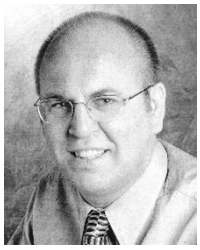

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