Proceedings of the International School and Conference on Photonics, PHOTONICA09

Long-Range Correlation in Atomic Vibration of Chicken Lysozyme Backbone

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Within this study we use methods such as spectral analysis that gives the spectral coefficient β, detrended fluctuations analysis that gives the scaling exponent α and the determination of Hurst exponent (H) to analyze the spatial series corresponding to the temperature factors of N, C-alpha, C and O atoms of 14 complexes of the chicken lysosyme. The mean values of the investigated parameters obtained for the 14 complexes are: $\beta = 1.779 \pm 0.086$, $\alpha = 1.382 \pm 0.009$ and $H = 0.916$. These values reveal long-range correlation in atomic vibrations corresponding to the chicken lysozyme backbone.

PACS numbers: 05.45.–a, 82.35.Pq, 87.15.hm

1. Introduction

Lysozyme is a protein that belongs to the hydrolases enzymatic class and catalyzes the hydrolytic cleavage of a chemical bond. In the human body the tears, mucus and blood contain lysozyme and it protects against bacterial infection by destroying the integrity of bacterial cell walls.

Hen egg white lysozyme is a 129 amino acids protein and serves to protect the proteins and fats that will nourish the developing chick [1]. There are a large variety of lysozymes belonging to different species, and their experimental atomic structures are hosted in the Protein Data Bank (PDB) [2].

There are some published data concerning different aspects of non-linear dynamics of lysozymes, such as its crystallization process [3], proton-exchange kinetics in lysozymes [4], lysozymes kinetics [5]. Other studies refer to the fractal aspects of lysozymes structures regarding their surfaces [6] and backbones [7], respective the fractal structure of lysozymes aggregates [8, 9]. Non-linear dynamics has been proven to apply for studies concerning the randomness of protein sequences [10–15], respective to protein folding and their conformational changes [16–21].

Within this study we analyze the correlation of atomic vibrations in the lysozymes main chain when it binds some ligands because this binding strongly affects the mobility of protein. It is largely recognized that both the atomic fluctuations and the fast collective motions in proteins can result in a spread of electron density over a range of space and therefore can be related to the atomic temperature factor (or B-factor), determined in an X-ray diffraction study of a protein crystal. The B-factor is defined by $B = 8\pi^2\langle u^2\rangle$, where $\langle u^2\rangle$ is the mean-square displacement of every atom averaged over the lattice [22]. For all the proteins having known crystallographic structures the temperature factors of their atoms are presented in the Protein Data Bank [2]. Analysis of B-factors gives us information about protein dynamics, the flexibility of amino acids and protein stability. The analysis of side chain mobility provides an index of flexibility for every amino acid. The published papers show that usually the active site residues have lower B factors suggesting that the active site residues are less flexible than the non-active site ones [23]. In our study we consider B-factor values of the atoms belonging to main chain (N, CA, C and O) of 14 macromolecular complexes of chicken lysozymes, the entry codes for these structural files being presented in Sect. 2. The spatial series of the changes in the temperature factors are then analyzed using non-linear methods: spectral analysis (SA), detrended fluctuation analysis (DFA) and calculation of the Hurst exponent.

2. Method

For this study we have randomly chosen a set of 14 lysozyme complexes with the following entry codes: 1zmy

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(chain L), 1ua6 (chain Y), 1mel (chain L), 1c08 (chain C), 1ic5 (chain Y), 1j1o (chain Y), 2yss (chain C), 1rjc (chain B), 1kiq (chain C), 1p2c (chain C), 1zvy (chain B), 1xfp (chain L), 3f6z (chain A) and 1ic4 (chain Y). Figure 1 illustrates the distribution of the B-factor values of the main chain atoms for the complex of chicken lysozyme with the heavy chain of camelid antibody (1rjc). We only consider the main chain atoms (N, CA, C and O) because these atoms are bound to each other in the protein backbone. Using B-factors values of the main chain atoms for the lysozymes complexes we have obtained spatial series and every series of data was subjected to the following investigation methods: the spectral analysis [24], the detrended fluctuation analysis [25] and the Hurst exponent calculation [26]. We make only a short description of these techniques here, a detailed description could be found by reading the literature quoted above.

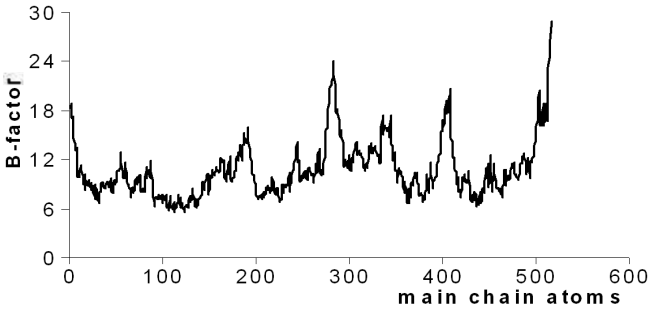

Fig. 1. The distribution of B-factor values along the main chain of chicken lysozyme complex with the heavy chain of camelid antibody (1rjc/chain B).

SA means that each series was subjected to a fast Fourier transform where the slope of the spectrum in double algorithmic scale, β, is called the spectral exponent. This method reveals the correlation of stationary fluctuations and the correlation introduced by the trend in the spectrum (a non-stationary contribution). In order to remove this non-stationary component, the DFA method is used. It allows to compute the scaling coefficient, α, which is related to the spectral exponent by [24]:

$$\beta_{\text{th}} = 2\alpha - 1. \tag{1}$$

The values of the two coefficients may be used to characterize the series of data: $\alpha = 0.5$ and $\beta = 0$ correspond to random series, $\alpha = 1$ and $\beta = 1$ corresponds to so-called "$1/f$" series (f is the frequency) and $\alpha = 1.5$ and $\beta = 2$ correspond to Brownian noise.

A third way to explore the tendency of time series is to calculate the Hurst coefficients [26] that provide a measure whether the data set is pure random or has underlying trends (there is some degree of autocorrelation). A value of $0 < H < 0.5$ indicates anti-persistence, $0.5 < H < 1$ indicates persistence in the series of data and $H = 0.5$ corresponds to Brownian noise [26].

3. Results and discussions

Within Figs. 2 and 3 we illustrate the implementation of the SA and DFA methods for B-factor values of the main chain atoms of chicken lysozyme complex with the heavy chain of camelid antibody. The linear fitting of the power spectrum, in double logarithmical plot, allows obtaining the spectral exponent from the slope of the line, $\beta = 1.637 \pm 0.091$ and it reveals long-range correlation within series of data.

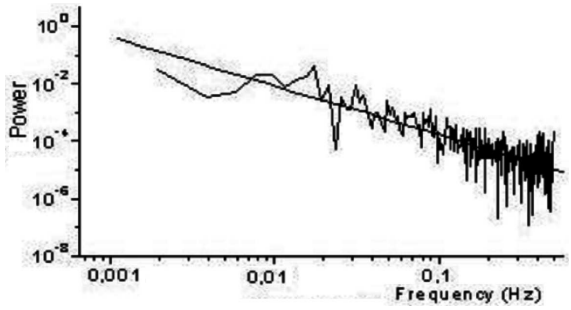

Fig. 2. Double logarithmical plot of the power spectrum for the series of B-factor values of the main chain atoms of chicken lysozyme complex with the heavy chain of camelid antibody (1rjc/chain B).

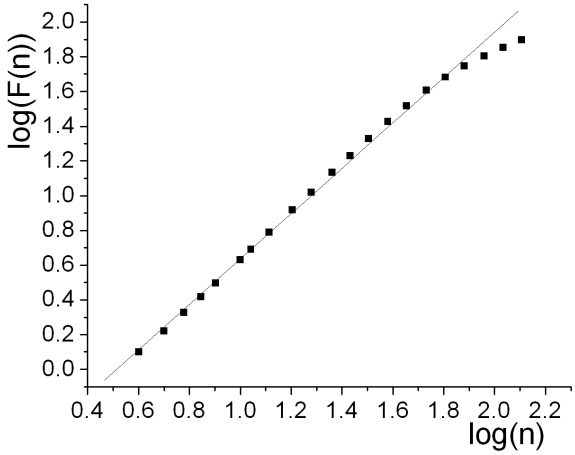

Fig. 3. The application of DFA method for the series of B-factor values of the main chain atoms of chicken lysozyme complex with the heavy chain of camelid antibody (1rjc/chain B).

The linear fitting in the DFA plot in Fig. 3 gives for the scaling coefficient the value $\alpha = 1.255 \pm 0.012$, also characterizing long-range correlation within the investigated data set. The presence of the long-range correlation in this case is also underlined by the calculated value of the Hurst exponent, $H = 0.843$. The calculated values of the α, β and H coefficients for all the series of data considered in this study are presented in Table. It also contains the theoretical value of the spectral exponent, calculated accordingly to Eq. (1).

TABLE
The values of the calculated coefficients for B-factor values along the main chain atoms of chicken lysozyme complexes.

PDB code/chain	β	α	$\beta_{\rm th} = 2\alpha - 1$	H
1zmy/chain L	1.736±0.079	1.256±0.003	1.512±0.006	0.947
1ua6/chain Y	1.766±0.089	1.401±0.003	1.802±0.006	1.000
1mel/chain L	1.671±0.093	1.396±0.009	1.792±0.018	0.637
1c08/chain C	1.788±0.093	1.355±0.005	1.710±0.010	0.994
1ic5/chain Y	1.715±0.097	1.334±0.008	1.668±0.016	1.000
1j1o/chain Y	1.848±0.081	1.452±0.004	1.904±0.008	0.985
2yss/chain C	1.987±0.076	1.454±0.015	1.908±0.030	0.910
1rjc/chain B	1.637±0.091	1.255±0.012	1.510±0.024	0.843
1kiq/chain C	1.853±0.080	1.419±0.008	1.838±0.016	0.973
1p2c/chain C	1.764±0.062	1.393±0.008	1.786±0.016	0.857
1zvy/chain B	1.892±0.087	1.428±0.012	1.856±0.024	0.926
1xfp/chain L	1.699±0.086	1.430±0.016	1.860±0.032	0.845
3f6z/chain A	1.682±0.100	1.429±0.015	1.858±0.030	0.927
1ic4/chain Y	1.870±0.088	1.330±0.009	1.660±0.018	0.983
mean values	1.779±0.086	1.382±0.009	1.764±0.018	0.916

We noticed that the values presented in Table are quite similar for all the complexes under study and they reveal long-range correlation within the investigated series of data. They also fall within the limits of values presented in specific literature for other proteins [7, 16–21]. The differences between β and $\beta_{\rm th}$ values are due to the non-stationary contributions.

If we compare the values of the spectral and scaling exponents obtained within this study with their values obtained in the case of correlation in the flexibility and hydrophobicity/hydrophilicity along the calcium binding proteins (CaBPs) and hydrolases chains [14, 15], we notice almost similar values for the spectral exponent but higher values for scaling exponent. The similarity of the spectral coefficients for the two studies are due to the fact that SA method does not allow the elimination of the non-stationary contribution within series of data. As DFA method removes the non-stationary contribution, higher values of scaling exponents obtained in this study show a stronger correlation in the vibration of the main chain atoms than in the flexibility and hydrophobicity properties along the protein chain.

Also, the values of exponents obtained in the present study are quite higher than those obtained for the series of the B-factors values for CA atoms of CaBPs and other investigated proteins [14]. This result is not surprising because CA atoms of the constitutive amino acids of protein are not directly connected in the chain as the N, CA, C and O atoms are.

4. Conclusions

The results presented in this study are in good agreement with published data concerning similar studies on other proteins [10–21] and they underline the sustainability of the hypothesis that the long-range correlation in both physicochemical and dynamical properties along the chain could be a general property of proteins. It means that analysis concerning conformational changes in the protein chain in relation to the active site must take into account that the local flexibility/rigidity is strongly correlated with the flexibility or rigidity of the entire protein.

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