

NON-LINEAR DYNAMICS OF BIOCHEMICAL REACTIONS IN CROWDED MEDIA

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Abstract

Classical kinetics is not applicable for biochemical reactions taking place in complex crowded media such as biological cell. In such a media we talk about fractal kinetics which implies a time dependence of the kinetic coefficients. Within this study we use the non-linear analysis methods (spectral analysis - SA, detrended fluctuation analysis - DFA) to analyze time series of rate coefficients describing diffusion-controlled enzymatic reactions obtained by Monte Carlo simulations in both two-dimensional (2D) and three-dimensional (3D) media without and with obstacles. The values of scaling exponents obtained with DFA method indicate uncorrelated data for media without obstacles, respective long-range correlation for media with obstacles, the correlation being stronger for 2D media. The values of the spectral coefficients, obtained with SA method, reveal that there is correlation within data sets, but it ceases to be of a power-law form.

Keywords: non-linear dynamics in chemical kinetics in crowded media, spectral coefficient, scaling exponent, Hurst coefficient.

1. Introduction

Nonlinear dynamics is interdisciplinary, its contribution to biology and medicine covering nonlinear self-organized dynamic at all major levels of biological organization, ranging from studies on enzyme kinetics to psychophysical experiments to humans. Cellular media are highly non-homogenous and crowded ones and these features lead to anomalous diffusion of substances and they modify action kinetics laws. There are in the literature many published papers concerning evidences of non-classical but fractal like kinetics for enzymatic reactions taking place in non-homogenous media obtained through computer simulations usually based on Monte-Carlo algorithm [1]-[11]. Therefore, as we know, there are only a few published papers concerning applications of nonlinear dynamics theory for studying deterministic diffusion and reactions processes [12]-[17].

2. Method and samples

Irreversible Michaelis - Menten mechanism for enzymatic reactions considers the following steps [18] $E + S \xrightleftharpoons[k_{-1}]{k_1} ES \xrightarrow{k_2} E + P$ where E is an enzyme, S is substrate, ES is enzyme-substrate complex, P is product and k_i are rate coefficients. Within these reactions only the first one $E + S \xrightarrow{k_1} ES$ is diffusion controlled because the two molecules E and S, need to diffuse in order to meet and react. So only k_1 rate coefficient is time dependent [1]-[6] and within this study we analyze this time series in order to detect long-range correlation in data sets. We consider both two dimensional (2D) and three dimensional (3D) media with the initial concentration of reactants $[E]=0.01$ for enzyme, $[S]=0.2$ for substrate and different obstacle densities: $[O]=0$, $[O]=0.12$, $[O]=0.25$, $[O]=0.37$. The obstacles density is always under the percolation threshold, $[O]_{pt}=0.403$ for a 2D media [1]. In order to analyze the long-range correlation in any time series we may use a few methods characteristic to nonlinear dynamics theory. In this study we use: spectral analysis (SA) method, detrended fluctuations analysis (DFA) method and the calculation of Hurst exponent [20], [21], [22]. Hurst exponent is calculated using Chaos Data Analyzer software package [19].

3. Results and Discussions

The values of k_1 rate for enzymatic reaction in two dimensional (2D) and three dimensional (3D) homogenous and crowded media are obtained through computer simulations using a Monte-Carlo algorithm which is presented elsewhere [2, 3]. In order to reveal the time dependence of k_1 rate coefficient we presented in figure 1 its time behavior for an enzymatic reaction taking place in a 2D media with obstacles to mimic the crowding. The parameters used in this simulation are: enzyme initial concentration $[E]=0.01$, substrate initial concentration $[S]=0.2$, obstacles concentrations $[O]=0.25$ and the lattice size 100×100 . All the values obtained for calculated parameters (spectral coefficient β , scaling exponent α and Hurst coefficient H) for all cases under investigation are presented in table 1.

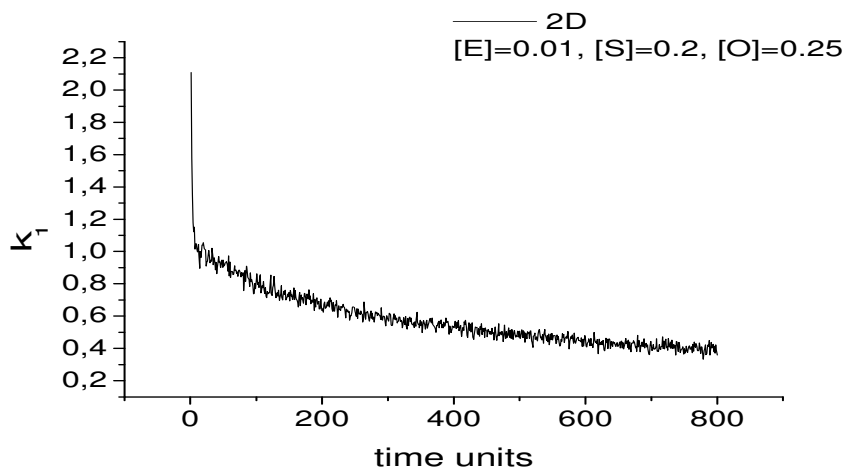


Figure 1 Time dependence of k_1 rate coefficient for an enzymatic reaction taking place in a 2D crowded media ($[E]=0.01$, $[S]=0.2$, $[O]=0.25$)

Table 1. The values of nonlinear parameters for the investigated data sets

Media Parameters, Obstacle density	2D			3D		
	β	α	H	β	α	H
[O]=0	1.419 ± 0.045	0.47 ± 0.007	0.9981	1.615 ± 0.046	0.528 ± 0.011	0.9997
[O]=0.12	1.376 ± 0.044	0.49 ± 0.007	0.9941	1.588 ± 0.042	0.541 ± 0.010	0.9997
[O]=0.25	1.342 ± 0.032	0.597 ± 0.007	0.9937	1.550 ± 0.037	0.538 ± 0.010	0.9996
[O]=0.37	1.264 ± 0.020	0.786 ± 0.007	0.9823	1.499 ± 0.030	0.571 ± 0.011	0.9992

4. Conclusions

The values of parameters presented in table 1 reveal non-randomness in investigated data sets. All values of the spectral coefficient deviate from unity and it means fractality self-similarity of the described process. This is also revealed by values of scaling exponents which deviate from 0.5, respective those of Hurst exponents which also deviate from 0.5 and tend to 1. We also notice increasing values of spectral coefficients and Hurst exponents with increasing obstacles density (increasing crowding). It is valid for both 2D and 3D media but there are noticeable differences in the values of these parameters for 2D and 3D media, they are always higher for 3D media.

Decreasing values of spectral coefficient and increasing values of scaling exponent indicate a stronger correlation within investigated time series. It means that the correlation between the values of k_1 rate coefficient increases with increasing crowding and it is stronger for 2D media in comparison to 3D ones. This last observation is related to the degree of

mixing within the system which is higher for 3D media and it favors diffusion process, respectively chemical reactions. These results also reveal the complex nature of biological systems at molecular level with strong consequences on the physicochemical processes at this level.

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