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DISPERSION OF REACTIVITY OF COPPER PROTEINS IN SOLUTIONS

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The redox reactions of superoxide dismutase and ceruloplasmin fit the simple kinetic schemes if the dispersion of their reactivities is accounted for by the time-dependent rate constants of the form $k(t) = Bt^{\alpha-1}$, $0 < \alpha \leqslant 1$. The lower the value of α the greater is the dispersion of reactivity. The limit of classical kinetics corresponds to $\alpha = 1$.

KEY WORDS: Dispersive kinetics, superoxide dismutase, ceruloplasmin.

The deviations of the kinetic data from the simple kinetic schemes may originate in many cases from the distribution of activation energy for reactions of biomolecules. Thus, e.g. the reduction and oxidation[1] of bovine SOD by H_2O_2 cf. Figure 1, or oxidation of human Cp by O_2, cf. Figure 2, can be regarded as pseudo-first-order processes described by the stretched exponentials

$$c/c_0 = \exp\left[-(t/\tau_0)^\alpha\right] \tag{1}$$

i.e. by a first-order kinetic equation with the time-dependent rate constant of the form[3]

$$k(t) = (\alpha/\tau_0)(t/\tau_0)^{\alpha-1} \equiv Bt^{\alpha-1} \tag{2}$$

The parameter $0 < \alpha \leqslant 1$ measures the dispersivity of the process.[3] The stretched exponential (1) can be regarded as the result of superposition of many simple exponential decays with probability density $f(\tau)$

$$\exp\left[-(t/\tau_0)^\alpha\right] = \int_0^\infty f(\tau)\exp(-t/\tau)\,d\tau \cdot \tag{3}$$

Then, by definition $\exp[-(t/\tau_0)^\alpha]$ is the Laplace transform of density $f(\tau)$ so that the latter is the inverse Laplace transform of $\exp[-(t/\tau_0)^\alpha]$. For large τ, which are of interest in kinetics, the inverse Laplace transform can be evaluated by saddle point calculations. The result is[4]

$$f(\tau) \sim \frac{(\alpha\tau)^{(2-\alpha)/2(1-\alpha)}}{\tau^2[2\pi\alpha(1-\alpha)]^{1/2}\,\tau_0^{\alpha/2(1-\alpha)}} \cdot \exp\left[-(1-\alpha)(\alpha\tau/\tau_0)^{\alpha/(1-\alpha)}\right]. \tag{4}$$

Distributions of reactant reactivity calculated according to equation (4) for the discussed data are presented in Figure 3. One point seen immediately is that dispersion of reactivity of copper ions in Cp exceeds markedly that in SOD. This is not surprizing, however, and of real interest are the origins of reactivity dispersion. Here we have

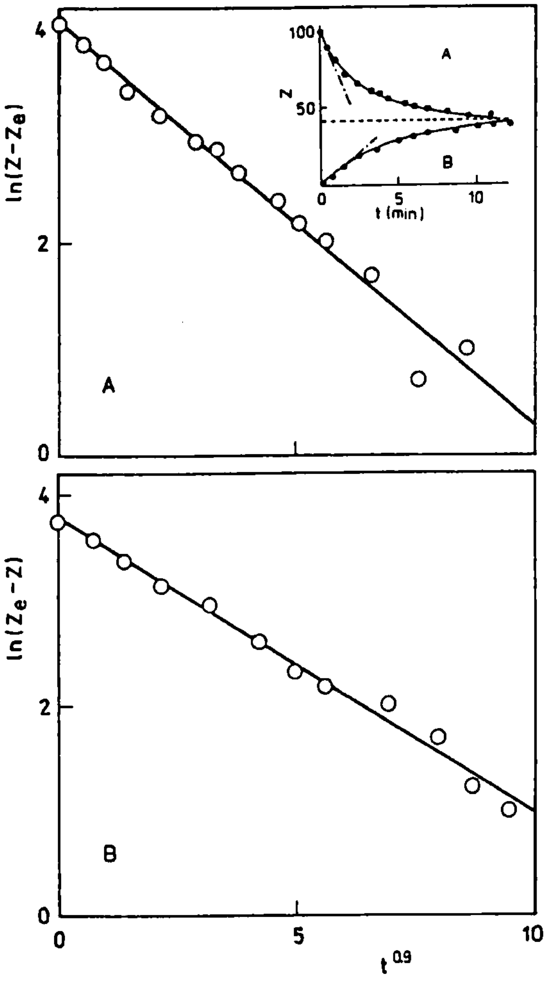

FIGURE 1 Reduction (A) and oxidation (B) of superoxide dismutase with excess of hydrogen peroxide fitted with the stretched exponentials, equation (1). The inset depicts the experimental data of Rigo *et al.*[1]

to recall that the traditional formalism for homogeneous reaction expresses the rate constant in terms of volume swept out by reacting molecules per unit time

$$k = dV/dt \tag{5}$$

In modelling by random walks dV/dt is substituted by the volume which the walker swept out in unit time[5]

$$k = b[dS(t)/dt] \tag{6}$$

where $S(t)$ is the mean number of distinct sites visited by a random walker on a lattice after time t. For regular three dimensional lattices ($D = 3$)

$$S(t) \sim t \tag{7}$$

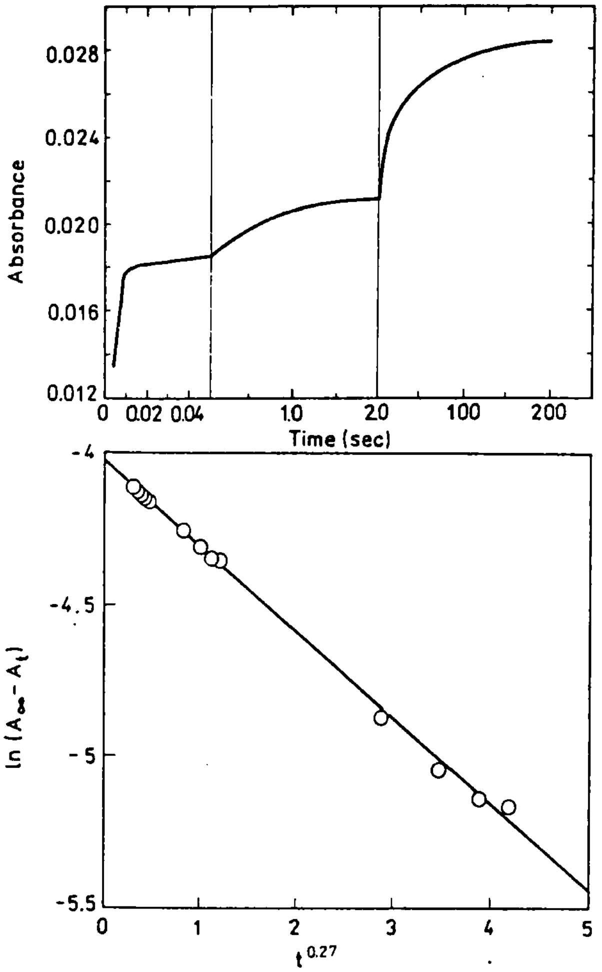

FIGURE 2 Oxidation of ceruloplasmin with excess oxygen. Above: the reaction curves presented by Carrico *et al.*[3] on a continuous time scale which contracts step-wise at the vertical line. Below: fit to the stretched exponential, equation (1).

and this, because of equation (6), leads to the classical kinetics, with k = const., valid for a "well-stirred" reactor.

It is hard to believe that these conditions are fulfilled by the above discussed systems. Three particular aspects of disorder may be considered:[6,7]

i) the spatial disorder modelled by random walks on self-similar structures, fractals, with

$$S(t) \sim t^{\bar{d}/2} \quad \bar{d} < 2 \qquad S(t) \sim t \quad \bar{d} > 2 \tag{8}$$

where $\bar{d}$ is the spectral dimension;

ii) the temporal disorder modelled by continuous time random walks

$$S(t) \sim t^{a} \qquad D = 3 \tag{9}$$

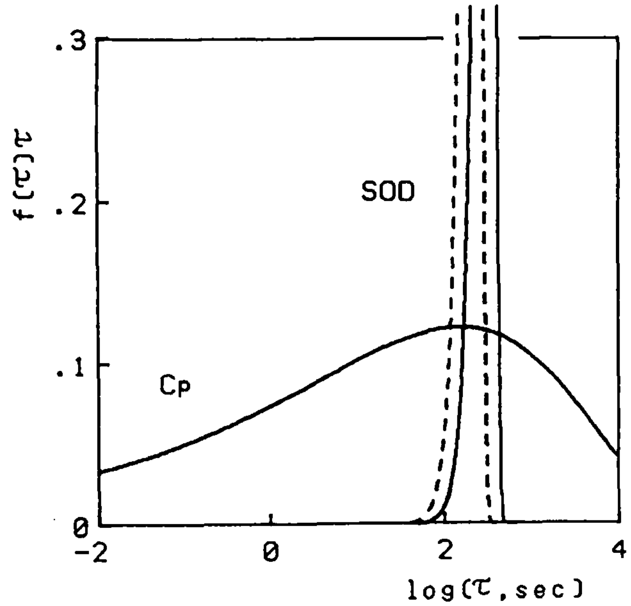

FIGURE 3 Dispersion of reactivity of copper ions in superoxide dismutase and ceruloplasmin calculated according to equation (4) for oxidation (solid lines) and reduction (dashed line).

with distribution of waiting times $\psi(t) \sim t^{-\alpha-1}$ which can be accounted for by barrier dispersion model;

iii) energetic disorder modelled by random walks on ultrametric spaces

$$S(t) \sim t^{\delta} \quad \delta < 1 \qquad S(t) \sim t \quad \delta > 1 \tag{10}$$

where $\delta = (kT/\Delta)$ ln b for consecutive energy levels differing by Δ and branching ratio b.

Although, at present, it is hard to discriminate among these possibilities, the barrier dispersion model[7] seems to be the most promising for further studies.

Acknowledgements

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