Title
Onsager coupling in enzymes

Journal
Biosystems, 8(4)

ISSN
0303-2647

Authors
Careri, G
Gratton, E

Publication Date
1977-04-01

DOI
10.1016/0303-2647(77)90037-5

BioSystems, 8 (1977) 185–186

ONSAGER COUPLING IN ENZYMES *

G. CARERI and E. GRATTON **
Istituto di Fisica, Università di Roma, Italy

(Received January 17th, 1977)

In a conference at Coral Gables in November 1973, on the occasion of the seventieth birthday of Lars Onsager, one of us, Careri (1974), proposed a mechanism of enzyme action grounded on the capability of the enzyme to correlate in time the statistical fluctuations of some macrovariables relevant for catalysis. This property can be expressed by a non-vanishing Onsager matrix, and Lars Onsager was very pleased with this picture because the enzymes being catalysts must work reversibly around equilibrium, and he said the "Onsager approximation" to be likely to hold in this case.

As a result of Lars Onsager's encouragement, the statistical time events which occur in enzymes have been critically reviewed by Careri et al. (1975) and the presence of nanosecond fluctuations in a dry lysozyme powder has been proved by oxygen quenching in the experimental stage by Careri, Gratton and Weber (unpublished). This experimental fact implies the existence of spontaneous fluctuations also in the active site of the enzyme, and, together with the known stochastic nature of the solvation effects, allow us to propose here an oversimplified model of the enzymatic action using one term of the Onsager matrix only, as follows.

Disregarding all the biochemical considerations about the stepwise chemical pathway, let us limit ourselves to the physical problem, namely that in order to overcome the free energy barrier the system must receive some free energy from the surrounding bath, and let us assume that this can be accomplished by a fluctuation. Molecular considerations not to be reviewed here, led to the conclusion that the major process by which the free energy can be exchanged between the macromolecule and the bath must be identified in the accommodation and release of the water molecules bound on the backbone amide groups which are accessible to the solvent. This bound water is known to amount up to 20–30% in weight of the macromolecule itself. Since the binding of the water molecule to the amide group increases the polar character of the peptide bond, and this induces a change in its conformation because of the increased planarity of the amide group, there is a possible propagation of these conformational changes from the surface of the enzyme to its active site, where even subtle conformational changes are essential to lower the free energy profile of the chemical reaction. Therefore a fluctuation of the bound water density at the surface can be coupled with a spontaneous conformational fluctuation at the active core, and this statistical coupling can be expressed by a non-vanishing Onsager coefficient, when the two statistical macrovariables are properly identified.

We propose here to identify the two fluctuating macrovariables as the concentration Z of the bound water at the surface, and as the reaction coordinate x at the active site. Then define

J = rate of the surface process = dZ/dt,

A = affinity of the surface processes = dG/dZ,

---

* Invited paper. Dedicated to the memory of Lars Onsager.

** Permanent address: Laboratorio Ricerche di Base, SNAM-Progetti, Monterotondo, Roma, Italy.

f = force acting on the substrate at the active site = dG/dx,
where G is the free energy and t the time. In order to work reversibly around equilibrium, we want the time averaged value of the dissipations function to vanish:

$$\overline{\phi} = \overline{f(dx/dt) + J \cdot A} = 0 \, .$$

Now, if we write the fluxes in the usual way:

$$dx/dt = L_{11} f + L_{12} A$$

$$J = L_{21} f + L_{22} A \, ,$$

in order for the enzyme to work as a mechanochemical engine, we want the Onsager coefficients: $L_{12} = L_{21} \neq 0$. By this we mean that the two fluctuating macrovariables Z and x are coupled, and since the largest amplitude free energy fluctuations are expected at the surface, these rare fluctuations let the system cross over the free energy barrier, a fact that we usually call catalysis.

Moreover, following Katchalsky and Oplatka (1969):

$$(f/A)_{dx/dt=0} = \left(-J \Big/ \frac{dx}{dt}\right)_{A=0}$$

namely if the equilbrium relaxation times of the processes occurring at the surface and those occurring at the active site are close to each other, we reach the limiting condition of strong coupling $-L_{12} = L_{11}$. The the free energy fluctuation initially present at the surface is completely transferred to the active site to force the system over the free energy barrier, namely:

$$dG/dx = dG/dZ \, .$$

The review by Careri et al. (1975) on the statistical events which occur in enzymes, suggests that indeed the relaxation times occurring at the surface (essentially the dielectric and nmr relaxation time of the bound water) and those occurring at the active site (essentially the segmental motions of the polymer and the changes in the hydrogen bonded network) are very close to each other and in the nanosecond range. Therefore the enzyme seems to operate as an ideal transducer of free energy from the bath to the active site. As already emphasized by Careri (1974) the above statistical treatment removes some inconsistencies which are found in the usual picture of the enzyme when described in terms of strain, distortion and conformational oscillations, if the reversibility constraint around equilibrium must also be satisfied.

References

Careri, G., 1974, The fluctuating enzyme, in: Quantum statistical mechanics in the natural sciences, (Plenum Publ. Co., New York) pp. 15–35.

Careri, G., Fasella P. and Gratton E., 1975, Time events in enzymes: a physical assessment. Crit. Rev. Biochem., pp. 141–164.

Katchalsky A. and Oplatka A., 1969, Mechano-chemical conversion, in: Handbook of Sensory Physiology, W.R. Lowenstein (ed.) (Springer-VErlag, Heidelberg), pp. 267–298.