A fully nonequilibrium concerted model for enzymes

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Although the concerted model (1) has been applied with some success to cooperative enzymes, it is actually an equilibrium model, whereas enzymatic phenomena of the greatest interest occur at nonequilibrium stationary states (where the net rate of catalysis is nonzero). The application of such an equilibrium binding model to a system with nonequilibrium stationary states is only valid when the enzyme can operate only in the "quasiequilibrium" regime (2). The concerted model will be generalized here so that all nonequilibrium aspects of catalysis are considered at the stationary state. Thus, not only equilibrium interactions but also interactions arising from dissipative effects will affect the binding and velocity response functions.

As a consequence, the Hill coefficient for substrate binding may be greater than the number of catalytic sites (which is in general not seen for any equilibrium model), or it may be < 1 ("negative cooperativity"), which is not predicted by the quasiequilibrium concerted model. In addition, the Hill coefficient for the conformational changes involved may be $>$ or < 1, whereas for the quasiequilbrium model it is always 1.

Two special cases which offer considerable simplification will also be presented: when the catalytic events occur much more rapidly than the conformational changes, the nonequilibrium effects on the Hill coefficient are seen only for substrate binding; when the conformational time scale is the faster, then the nonequilibrium effects are seen only for the conformational changes.

1) Monod, J., Wyman, J. and Changeux, J. (1965), J. Mol. Biol., 12, 88.
2) Hill, T.L., (1977), Proc. Natl. Acad. Sci. USA, 74, 3632.