J. theor. Biol. (1991) **152,** 39-40

How Much Effect on Free Metabolite Concentrations does Channelling Have?

It would not be appropriate for me, as convener of this discussion, to express any forcible opinions about the controversial aspects of metabolite channelling. Moreover, as an outsider in the field, or at best a newcomer to it, I realize that in expressing any view at all I run the risk of exposing my ignorance without much illuminating the subject. I shall simply pose a question, therefore, as it seems to me that not all of the pertinent questions about the physiological significance of channelling have been addressed. Although there has been abundant discussion of the evidence that channelling occurs, and in her article Ovádi (1991) refers to much of this, there has been much less discussion of the physiological benefits that channelling can provide. Possibly these benefits have seemed to many workers to be obvious, but I have not succeeded in understanding them deeply enough to find them obvious.

Atkinson (1969, 1977) pointed out that a system of highly complex composition could be tolerated by the limited solvent capacity of water only if the concentrations of solutes are maintained at low values. Ovádi (1991) refers to this in her review, and other authors have done likewise, in most cases with the implication that metabolite channelling provides the possibility of achieving these low concentrations, though Atkinson himself did not draw this conclusion; he argued instead that the limited solvent capacity of water required the evolution of highly efficient enzymes capable of removing intermediates rapidly.

Consider, for example, the following two statements: first, "Atkinson's (1969) argument of too little water to solvate all the necessary metabolites, is not *eo ipse* convincing: in a non-channelled pathway at steady state, evolution could well reduce all metabolite concentrations by a factor of say 10, by reducing all Michaelis constants by that same factor, or by increasing all V_{max}s except that of the first enzyme" (Westerhoff, 1991); second, "It is also evident that a dynamic chemical system operating at typical biological rates can be constructed with all intermediates at concentrations in the nanomolar-to-millimolar range only by the use of very effective catalysts; it is noteworthy that many enzymes catalyze reactions at rates of 10^{10} to 10^{16} times those of corresponding nonenzymatic reactions" (Atkinson, 1977). It will be evident that Westerhoff's response to "Atkinson's argument" is itself similar to Atkinson's argument!

Elsewhere (Cornish-Bowden, 1991) I have pointed out that the existence of a channel does not guarantee a lower free concentration of the by-passed intermediate than one would have if the channel did not exist. Depending on how one constructs the model, one can set up conditions where the appearance of a channel increases this free concentration, where it decreases it, or where it leaves it unchanged. The model with this last characteristic assumes that increasing the activity of the channel is compensated for by decreasing the activity of the route via free intermediate so

0022-5193/91/170039+02 $03.00/0

as to maintain a fixed flux to final product, and it ignores the possibility that the free intermediate may participate in other reactions; it seems to me the most realistic model for analysing the possibility that channelling can overcome the limited solvent capacity of water. This sort of simulation cannot, of course, prove that channelling cannot have this effect, because it is always possible that a simulation has failed to consider the appropriate conditions. It does suggest, however, that if channelling is to be regarded as mechanism for decreasing free concentrations the conditions in which it is able to do this need to be defined.

Centre de Biochimie et de Biologie Moléculaire,
Centre National de la Recherche Scientifique,
13402 *Marseille Cedex* 9, *France*

ATHEL CORNISH-BOWDEN

REFERENCES

ATKINSON, D. E. (1969). *Curr. Top. Cell. Reg.* **1,** 29–43.
ATKINSON, D. E. (1977). *Cellular Energy Metabolism and its Regulation.* New York: Academic Press.
CORNISH-BOWDEN, A. (1991). *Eur. J. Biochem.* **195,** 103–108.
OVÁDI, J. (1991). *J. theor. Biol.* **152,** 1–22.
WESTERHOFF, H. V. (1991). *J. theor. Biol.* **152,** 123–130.