

## Letters to the Editor

### Problems In Biochemistry and Biophysics

The considerations in the paper by J. S. Shiner have no relevance to real problems in biochemistry and biophysics. These problems originate, experimentally, in observed fluxes. The models created to represent the observations will necessarily contain cycles of not less than two states to account for these real fluxes. There is no way to model a real flux with a one-state cycle. Furthermore, a two-state cycle representing a real flux cannot be reduced to a one-state cycle and still represent the flux. Hence, from an operational point of view, the problem Shiner treats is irrelevant. This, of course, does not detract from its possible interest in relation to more abstract questions.

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### Response to Terrell L. Hill

T. L. Hill seems to have understood my paper but simultaneously to have missed an important point. Yes, real fluxes must be accounted for by cycles with at least two states. However, if the individual transitions of these cycles occur on a time scale which is too fast to be observed, it will not be possible to achieve a model description of these cycles based on experiment, since to do so would require knowledge of the transitions. This may be so even though population properties may be accurately described on the slower time scale of the possible observations.

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**Comments on J. S. Shiner Response**

Any enzymatic cycle, *no matter how fast*, leaves a record of its activity in the form of small molecule chemical reaction or transport in the surrounding solution or solutions. Any such observed record must be modelled by at least a two-state cycle in the kinetic diagram. Very large rate constants can be used in the cycle, if appropriate, but the cycle has to be included in the diagram if the diagram is to represent the observed facts.

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