

**Why are enzymes so small?  
or  
Why do biochemists ask 'Why are enzymes so big?'**

For at least 20 years, and probably for much longer, the question 'why are enzymes so big?' has been a favourite in oral examinations. It is often discussed by biochemists, for example in the pages of *TIBS*<sup>1-3</sup>. Many of the proposed answers to the question are perfectly sensible and I have no quarrel with them. My purpose is not to discuss possible answers but the question itself: why does it get asked, and why does it virtually never receive the response that enzymes are not especially large when judged by the standards we use in everyday life?

Hexokinase D from rat liver, the enzyme that has attracted much of my interest over the past decade, has a molecular mass of about 48 kDa, around 70 times the combined molecular masses of glucose and MgATP. Although some enzymes, such as catalase, would give a much larger ratio, whereas others, such as ribonuclease, would give a much smaller one, a value of 70 is not untypical for an enzyme of intermediary metabolism. Is a ratio of 70, which we should really think of as a ratio of volumes rather than masses if we are comparing sizes, particularly large?

The office in which I am preparing this article has a floor area of 7.4 m<sup>2</sup> and a height of 2.3 m. Thus its volume is about 17 m<sup>3</sup>, or around 250 times the volume of an average biochemist. It is not an unusually large office, and I would suspect that a factor of around 250 would be quite typical for most of the offices occupied by the people who ask the question 'why are enzymes so big?' Yet they do not ask 'why do biochemists work in such large offices?' Nor do they ask, watching the removal of the liver from a rat of perhaps 0.3 kg (volume about 300 ml), 'why do biochemists obtain their enzymes from such microscopic animals?'

I believe that the question properly belongs in the realm of psychology, not biochemistry. When we consider things in the everyday world that we can handle, like rooms or rats, we tend to consider sizes in relation to linear dimensions rather than volume or mass. Consequently we do not consider a room of 250 times our own volume as large, because this factor corresponds to only a little more than a factor of six in linear terms. For the same reason, we ought not to be impressed by a ratio of 70 when comparing the molecular mass of an enzyme with those of its substrates: such

a ratio is barely more than a factor of four in linear dimensions.

#### References

- 1 Kell, D. G. (1982) *Trends Biochem. Sci.* 7, 349
- 2 Payens, T. A. J. (1983) *Trends Biochem. Sci.* 8, 46
- 3 Sreere, P. A. (1984) *Trends Biochem. Sci.* 9, 387-390

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DOCTOR CORNISH-BOWDEN! YOU - OF ALL PEOPLE -  
ASK "WHY IS THE COFFEE-CUP SO SMALL?!"

*Trends in Biochemical Sciences*  
**11, 286 (1986)**