

**Table 12.4** Metabolite concentrations and  $K_M$ 's for some glycolytic enzymes<sup>d</sup>

Enzyme	Source	Substrate	Concentration ( $\mu M$ )	$K_M$ ( $\mu M$ )	$K_M/[S]$
Glucose 6-phosphate isomerase	Brain	G6P	130	210	1.6
	Muscle <sup>b</sup>	G6P	450	700	1.6
		F6P	110	120	1.1
Aldolase	Brain	FDP	200	12	0.06
	Muscle <sup>c</sup>	FDP	32	100	3.1
		G3P	3	1000	333
		DHAP	50	2000	40
Triosephosphate isomerase	Erythrocyte <sup>d</sup>	G3P	18	350	19
	Muscle <sup>e</sup>	G3P	3	460	153
		DHAP	50	870	17
Glyceraldehyde 3-phosphate dehydrogenase	Brain	G3P	3	44	15
	Muscle <sup>f</sup>	G3P	3	70	23
		NAD	600	46	0.08
		P <sub>i</sub>	2000		>10 <sup>8</sup>

<sup>a</sup>Abbreviations: G6P = glucose 6-phosphate, F6P = fructose 6-phosphate, FDP = fructose 1,6-diphosphate, G3P = glyceraldehyde 3-phosphate, DHAP = dihydroxyacetone phosphate, P<sub>i</sub> = orthophosphate, 1,3DPG = 1,3-diphosphoglycerate, 3PG = 3-phosphoglycerate, 2PG = 2-phosphoglycerate, PEP = phosphoenolpyruvate, Pyr = pyruvate, Lac = lactate (all D-sugars); Gly-P = L-glycerol phosphate. Mouse brain enzymes and mouse brain metabolites from O. H. Lowry and J. V. Passonneau, *J. Biol. Chem.* **239**, 31 (1964). Human erythrocyte metabolites from S. Minakami, T. Saito, C. Suzuki, and H. Yoshikawa, *Biochem. Biophys. Res. Commun.* **17**, 748 (1964). Human erythrocyte enzymes: see below. Rat diaphragm metabolites from E. A. Newsholme and P. J. Randle, *Biochem. J.* **80**, 655 (1961); H. J. Hohorst, M. Reim, and H. Bartels, *Biochem. Biophys. Res. Commun.* **7**, 137 (1962). Rabbit skeletal muscle enzymes: see below. Metabolite concentrations were calculated on an intramolecular water content of 60% for brain and muscle cells, and 70% for erythrocytes. No allowance has been made for compartmentation in the muscle and brain cells, but gross metabolite concentrations are usually close to those in the cytosol [A. L. Greenbaum, K. A. Gumaa, and P. McLean, *Archs. Biochem. Biophys.* **143**, 617 (1971)]. The values for mouse brain are those immediately on decapitation. The use of peak levels does not cause significant differences.

<sup>b</sup>From J. Zalitis and I. T. Oliver, *Biochem. J.* **102**, 753 (1967).

<sup>c</sup>From W. J. Rutter, *Fedn. Proc.* **23**, 1248 (1964); P. D. Spolter, R. C. Adelman, and S. Weinhouse, *J. Biol. Chem.* **240**, 1327 (1965).

<sup>d</sup>From A. S. Schneider, W. N. Valentine, M. Hattori, and H. L. Heins, *New Engl. J. Med.* **272**, 229 (1965).

<sup>e</sup>From P. M. Burton and S. G. Waley, *Biochem. Biophys. Acta* **151**, 714 (1968).

<sup>f</sup>From M. Oguchi, E. Gerth, B. Fitzgerald, and J. H. Park, *J. Biol. Chem.* **248**, 5571 (1973).

<sup>g</sup>The  $K_M$  of ~6 mM for P<sub>i</sub> refers to high G3P concentrations where the acylenzyme accumulates.

Enzyme	Source	Substrate	Concentration ( $\mu M$ )	$K_M$ ( $\mu M$ )	$K_M/[S]$
Phosphoglycerate kinase	Brain	1,3DPG	<1	9	>9
		ADP	1500	70	0.05
	Erythrocyte <sup>h</sup> Muscle <sup>i</sup>	3PG	118	1100	9.3
		3PG	60	1200	200
Phosphoglycerate mutase	Brain	ADP	600	350	0.6
		3PG	40	240	6
	Muscle <sup>j</sup>	3PG	60	5000	83
Enolase	Brain	2PG	4.5	33	7
	Muscle <sup>k</sup>	2PG	7	70	10
Pyruvate kinase <sup>l</sup>	Erythrocyte <sup>m</sup>	PEP	23	200	9
		ADP	138	600	4.4
Lactate dehydrogenase	Brain	Pyr	116	140	1.2
		Pyr	51	59	1.2
	Erythrocyte <sup>n</sup>	Lac	2900	8400	2.9
		NADH	0.01 <sup>o</sup>	10 <sup>p</sup>	100
		NAD	33	150	4.6
Glycerol phosphate dehydrogenase	Mouse	Gly-P	170	37	0.22
	Muscle <sup>q</sup>	Gly-P <sup>r</sup>	220	190	0.9
		DHAP	50	190	3.8

*Biochem. J.* **143**, 353 (1974)]. Note: The unhydrated forms of G3P and DHAP are probably the substrates of the reactions. The concentrations tabulated are for both the hydrated and the unhydrated forms, but the values of  $K_M$  for the unhydrated forms and their concentrations are overestimated in the same ratio [D. R. Trentham, C. H. McMurray, and C. I. Pogson, *Biochem. J.* **114**, 19 (1969); S. J. Reynolds, D. W. Yates, and C. I. Pogson, *Biochem. J.* **122**, 285 (1971)].

<sup>h</sup>From A. Yoshida and S. Watanabe, *J. Biol. Chem.* **247**, 440 (1972).

<sup>i</sup>From D. R. Rao and P. Oesper, *Biochem. J.* **81**, 405 (1961).

<sup>j</sup>From R. W. Cowgill and L. I. Pizer, *J. Biol. Chem.* **223**, 885 (1956); S. Grisolia and W. W. Cleland, *Biochemistry* **7**, 1115 (1968).

<sup>k</sup>From F. Wold and R. Barker, *Biochim. Biophys. Acta* **85**, 475 (1964).

<sup>l</sup>It is debatable whether or not this is a control enzyme; PEP is certainly well below the  $K_M$  in any case. The data quoted are for the presence of 500- $\mu M$  FDP, in which case Michaelis-Menten kinetics hold. In the absence of FDP, sigmoid kinetics holds with a  $K_{0.5}$  of 650  $\mu M$ .

<sup>m</sup>From S. E. J. Staal, J. F. Koster, H. Kamp, L. van Milligan-Boersma, and C. Veeger, *Biochim. Biophys. Acta* **227**, 86 (1971).

<sup>n</sup>From J. S. Nisselbaum and O. Bodansky, *J. Biol. Chem.* **238**, 969 (1963).

<sup>o</sup>Calculated from the lactate/pyruvate ratio, assuming NAD and NADH at equilibrium, and using an equilibrium constant of  $1.11 \times 10^{-4}$ . [From R. L. Veech, L. V. Eggleston, and H. A. Krebs, *Biochem. J.* **115**, 609 (1969).]

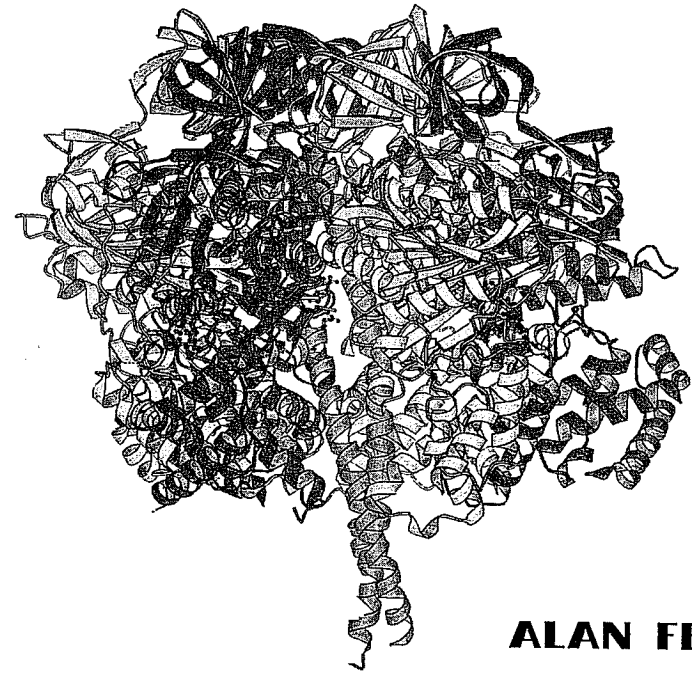
<sup>p</sup>From S. Rapoport, *Essays in Biochemistry* **4**, 69 (1969).

<sup>q</sup>From T. P. Fondy, L. Levin, S. J. Sollohub, and C. R. Ross, *J. Biol. Chem.* **243**, 3148 (1968).

<sup>r</sup>From R. M. Denton, R. E. Yorke, and P. J. Randle, *Biochem. J.* **100**, 407 (1966).

# STRUCTURE AND MECHANISM IN PROTEIN SCIENCE

A Guide to  
Enzyme  
Catalysis  
and Protein  
Folding



**ALAN FERSHT**

**Cover Illustrations:**

**Front** Structure of the  $F_1$ -ATPase and the Boyer "binding change mechanism" (Courtesy of Dr. A. G. W. Leslie and Dr. J. E. Walker.)

**Back** *Top*: A folding funnel. [From J. N. Onuchic, N. D. Socci, Z. Luthey Schulten, and P. G. Wolynes, *Folding and Design* 1, 441 (1996).] *Bottom*: Structures of the denatured, intermediate, major transition, and native states for folding of barnase from molecular dynamics simulations that were benchmarked by  $\Phi$  values and NMR experiments. [Data from C. J. Bond, K. B. Wong, J. Clarke, A. R. Fersht, and V. Daggett, *Proc. Natl. Acad. Sci. USA* 94, 13409 (1997).]



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