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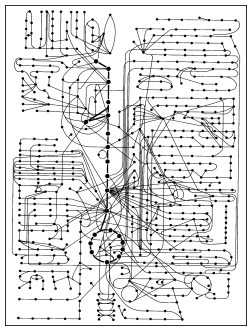

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Front cover artwork: The maze of intermediary metabolism, reactions indicated by lines and metabolites by dots. © 1989 from *Molecular Biology of the Cell*, 2E, by Alberts et al. Reproduced by permission of Garland Science/Taylor & Francis LLC.

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Preface

If you want to make explorations of physiological and biochemical reactions in a reproducible biological system, yeast can usually do it better.

Britton Chance (1913–2010)[1]

ADVANCED OR SPECIALIZED BOOKS ON INTERMEDIARY metabolism are many,[2] but elementary and general ones are few. The present volume is based on *Saccharomyces cerevisiae*, "yeast," the long-studied eukaryotic microbe, and also illustrates common aspects of metabolism throughout biology. It deals with pathways, mutants, and methods and touches on history[3] and gaps in knowledge. The book is meant as a handbook for those who work with yeast to place reactions in context or as a basic text on metabolism. It assumes a familiarity with general biochemistry, but Chapter 2 reviews enzyme and cofactor reactions. Matters not dealt with include enzyme mechanisms, cell biology, gene expression, protein modification, macromolecule turnover, single cells, biofilms, rhythms, theory, and how metabolism came to be. The book accepts the conventions that biochemical pathway is a useful notion, energetics employs delocalized ion gradients, and metabolites freely diffuse within compartments. None is set in stone. Metabolism is a work in progress, with nominally straightforward issues hard to address in vivo, including metabolite and enzyme locations and interactions, fluxes between compartments, and direct assignment of enzyme function.

Basic description is given in the text; boxes provide detail, examples, techniques, and history. Some attention is paid to jargon. Shorthand is avoided, but in biochemistry that has its limits and the common abbreviations, like ATP for adenosine triphosphate, are used. (One small exception is that, although the reduced pyridine nucleotides are as usual named NADH or NADPH, in their reactions the term NAD(P)H2 will stand for NAD(P)H+H^+.) In general, notation follows the custom in Michal and elsewhere (see the list in note 4) that in chemical names "P" stands for phosphate (as in glucose-6-P) and "PP_i" for pyrophosphate, and in chemical formulas -OP stands for $-OPO_3H_2$ with charge at pH 7 of phosphate or carboxyl or amino groups usually not indicated. For proteins, enzyme or subunit, the symbol employed matches the gene name (as in Xyz1, not italicized and not Xyz1p; the number is included unless the context is the several Xyz proteins). An index of proteins lists where the protein is found in the text, its EC designation, and its

cell location, albeit uncertain or incomplete. By this listing, approximately 800 identified proteins in *S. cerevisiae* belong to intermediary metabolism.

When possible, mutant phenotypes—sometimes a nutritional requirement—are mentioned or implied. Here "mutant" usually refers to loss of the protein or its function, often the null mutant—a blunt tool. Most steps of intermediary metabolism are not essential, as defined by the mutant not growing on enriched medium with glucose; among those assigned as essential, some do grow on another medium. Conversely, apparently normal growth of a mutant does not show that an enzyme is unimportant: it may be normally employed for an essential step but other enzymes are adequate in its absence. The distinctions also depend on how closely growth or metabolism is examined. Explanations of growth impairments can be complicated.

The references include reviews and research articles. I have also depended on textbooks[4]; on the astonishing resources MedLine, the *Saccharomyces* Genome Database, and Wikipedia; on computer support from K. Ketterer; on the Countway Library of Medicine; and on other support from J. Hillman and J. Mekalanos.

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Dan Fraenkel

Boston, Massachusetts
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FOOTNOTES

[1] Bacila M, Horecker BL, Stoppani AOS, eds. 1978. *Biochemistry and genetics of yeasts: Pure and applied aspects*, p. 31. Academic, New York.

[2] Some in English include Cramer WA, Knaff DB. 1990. *Energy transduction in biological membranes: A textbook of bioenergetics*. Springer-Verlag, New York; Fell D. 1997. *Understanding the control of metabolism*. Portland Press, London; McMurry J, Begley T. 2005. *The organic chemistry of biochemical pathways*. Roberts & Co., Englewood, CO; Newsholme EA, Start C. 1973. *Regulation in metabolism*. Wiley, New York; Stein WD. 1990. *Channels, carriers, and pumps. An introduction to membrane transport*. Academic, San Diego; Stephanopoulos GN, Aristidou AA, Nielsen J. 1998. *Metabolic engineering: Principles and methodologies*. Academic, San Diego; Tzagoloff A. 1982. Mitochondria. Plenum, New York; Walsh C. 2006. *Posttranslational modification of proteins: Expanding nature's inventory*. Roberts & Co., Englewood, CO; Westerhoff HV, van Dam K. 1987. *Thermodynamics and control of biological free-energy transduction*. Elsevier, Amsterdam; Zimmermann FK, Entian KD. 1997. *Yeast sugar metabolism: Biochemistry, genetics, biotechnology, and applications*. CRC Press, Boca Raton, FL.

[3] See Fruton JS. 1999. *Proteins, enzymes, genes: The interplay of chemistry and biology*. Yale University Press, New Haven, CT; Florkin M. 1975, 1977, 1979. *A history of biochemistry*, Vols. 31–33 in *Comprehensive biochemistry* (ed. Florkin M, Stotz EH). Elsevier, Amsterdam, and Oxford, New York; and the reviews by (mainly) Barnett JA. 1998–2008. In (the journal) *Yeast*, Vols. 14, 16, 18–22, 24, and 25. (See Barnett JA, Barnett L. 2011. *Yeast research: A historical overview*. ASM Press, Washington, DC.)

[4] Including Mahler HR, Cordes EH. 1966. *Biological chemistry*. Harper & Row, New York; Michal G, ed. 1999. *Biochemical pathways. An atlas of biochemistry and molecular biology*. Wiley, New York; White D. 2000. *The physiology and biochemistry of prokaryotes*, 2nd ed. Oxford University Press, New York.