4

Central Metabolism 1

Glycolysis and Fermentation

INTRODUCTION

The glycolytic pathway, shown in Figure 4-1, is the main route of hexose use throughout the living world, including yeast and human. Organisms that do not have this pathway use pieces of it, with the reactions between glyceraldehyde-3-P and pyruvate being near universal. Most of the same reactions—indeed, the same enzymes—are also employed (although in the opposite direction from catabolism) in gluconeogenesis and in growth on respiratory substrates such as ethanol, and—regardless of carbon source—at least six of the pathway's nine intermediates are starting compounds for biosynthetic pathways. In these respects, it is the paradigmatic central metabolic route. In growth of yeast in a glucose-replete medium, the glycolytic flux is by far the highest of any metabolic pathway: Counted as the rate of provision of ATP, which is 1 per pyruvate made, that flux is approximately 20 times as high as synthesis of peptide bonds. For obvious reasons, glycolysis is called a "pathway." Whether it arose as such is another matter, with perhaps its lower reactions coming first and in the gluconeogenic direction (Box 4-1).

Because of wide familiarity with this pathway, the basis of so much biochemistry, and because Chapter 1 has sketched the pathway and its major uses in both directions, the format of the present chapter is first to describe the individual steps: transport plus the 10 reactions between glucose and pyruvate (Fig. 4-1); then fermentation, the oxidation/reduction balance giving mainly ethanol; and then some analyses dealing with the whole pathway. The exception is first to point out that glycolysis mutants have not been major subjects in microbial genetics, in part because in yeast and many other microbes glucose is the usual default permissive carbon source, so deficiency mutants would be considered lethal and studies might require conditional mutants (as with studies of essential genes). Indeed, in yeast, null mutants for glycolytic steps with single isozymes are usually scored as lethal. Furthermore, in most of those cases, because the same enzyme is needed in both glycolysis and gluconeogenesis, a mutant unable to grow on glucose should not grow on ethanol either.

In fact, however, glycolysis mutants could be obtained by ordinary forward genetics, often by the use of two carbon sources whose catabolism supplied both sides of the block (e.g., glycerol plus ethanol) or sometimes with rich media, which might supply end products.