admittedly neither comprehensive nor mutually exclusive:

How are the events of the cell cycle coordinated? How does the cell assure that any two discontinuous cell cycle events such as deoxyribonucleic acid (DNA) synthesis and nuclear division always occur in the proper order?

How is cell division controlled? How does the cell arrest the mitotic cell division cycle and commence upon an alternative developmental program such as sexual conjugation, meiosis, or stationary phase?

How is growth integrated with division? How does the cell accomplish the precise doubling of all of its macromolecular components between two consecutive cell cycles under conditions of balanced growth?

The material selected for the present review was chosen in large part because of its relevance to one or more of these questions. Although it will not be possible at the present time to provide satisfying answers to any of these questions, it will be possible during the course of this review to rephrase them. Whether that accomplishment represents an exercise in semantics or a measure of progress, the reader must decide.

The discontinuous events that occur once during each cell cycle constitute *landmarks* of cell cycle progress by which we can assess a cell's position. The landmarks of the *S. cerevisiae* cell cycle will be discussed in greater detail below, but it may be useful to consider their temporal order at this time (Fig. 1). For reasons that will become apparent later it is appropriate to consider the cycle as commencing with an unbudded cell in the G1 interval of the cycle. The nucleus contains a single-spindle plaque, a structure embedded in the nuclear membrane from which microtubules arise. Three events, whose precise temporal order has not been determined, mark the end of the G1 interval: spindle plaque duplication, the initiation of DNA synthesis, and the emergence of the bud. The DNA synthetic interval or S period constitutes about 25% of the cycle. The spindle plaques separate to form the complete spindle, and the bud grows in size throughout the remainder of the cycle. The end of G2 is marked by the migration of the nucleus to the neck of the cell where it undergoes the first stage of nuclear division, medial nuclear division, concomitant with the elongation of the spindle microtubules. The second stage of nuclear division, late nuclear division, is followed by cytokinesis, or cell membrane separation, which is followed in turn by cell wall separation. This event completes the cycle with the production of two unbudded cells. A diploid cell growing at the optimal temperature, 30 C, may complete a cycle in about 100 min. Although the literature on the *S. cerevisiae* cell cycle will be extensively referenced below, it is appropriate to acknowledge at this point that much of our current understanding of the yeast cell cycle is the result of pioneering research carried out for several years in the laboratories of H. O. Halvorson, C. F. Robinow, and D. H. Williamson.

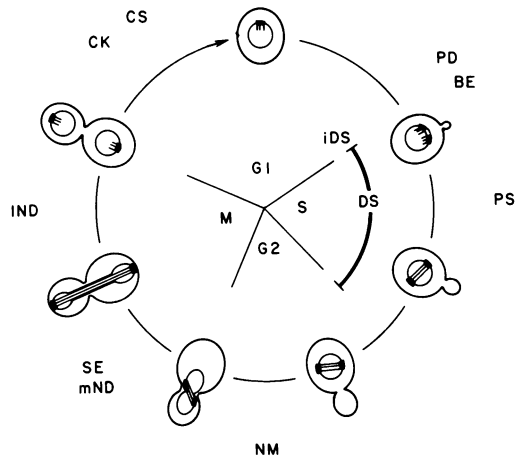

FIG. 1. *Landmarks of the S. cerevisiae cell division cycle. Abbreviations: PD, plaque duplication; BE, bud emergence; iDS, initiation of DNA synthesis; DS, DNA synthesis; PS, plaque separation; NM, nuclear migration; mND, medial nuclear division; SE, spindle elongation; lND, late nuclear division; CK, cytokinesis; CS, cell separation. Distance between events does not necessarily reflect interval of time between events.*

SYNCHRONOUS CULTURES

Assay of Landmarks

The experimental analysis of the cell cycle frequently requires synchronous cultures and a number of methods employing either induction or selection (114) have been devised to achieve partially synchronous division of *S. cerevisiae*. In such experiments, it is necessary to follow at least one landmark as a measure of the degree of synchrony, and more than one is preferable. A brief discussion of the synchrony techniques available for yeast can be usefully integrated with another methodological consideration, how each of the landmarks are assayed.

The most convenient landmark is bud emergence because it can be monitored by direct visual examination and there is essentially no subjective element involved in distinguishing an unbudded from a budded cell.

DNA synthesis has also been used as a measure of synchrony. However, because the S period occupies a significant but not easily determined portion of the cycle, this measurement is inherently less accurate than that of