of internal termination sites may reflect the evolution of gene clusters from independent genes and they may be ignored by the rho factor in the conditions prevailing *in vivo*.

An important difference between the conditions of transcription *in vitro* and *in vivo* is that translation proceeds simultaneously with transcription in the cell, but the messengers are not translated *in vitro*. One consequence of the failure of simultaneous transcription and translation in the cell is polarity; mutants which cause termination of protein synthesis in one gene change the properties of messenger RNA representing subsequent genes. Two theories have been proposed to explain this polarity. One explanation is that messenger is synthesized beyond the mutant site but is degraded by cellular nucleases because it is no longer being translated; the other postulates that translation is needed if transcription is to continue so that the enzyme ceases RNA synthesis at or soon beyond the mutant site (see *Nature New Biology*, **232**, 161; 1971).

Polarity can be caused by the presence of nonsense mutations and by the insertion of foreign DNA into the operon. Insertion mutants differ from nonsense mutants in that they are always extremely polar and their polarity does not show the dependence on position within the gene characteristic of nonsense mutations. De Crombrugghe *et al.* have found that one such insertion mutant where the insertion is located close to the beginning of the galactose genes is transcribed normally *in vitro* by RNA polymerase. But if rho factor is added to the incubation, transcription terminates within the inserted sequence. The insertion is very sensitive to rho and reacts at even the lowest concentrations of the factor.

In this situation, polarity results from rho-dependent termination. Does a similar mechanism explain the polarity of nonsense mutations, perhaps, for example, because nonsense codons constitute part of the DNA sequence recognized by rho factor? Polar nonsense mutants in the galactose operon proved to have no effect on transcription, however, in either the absence or presence of rho. This implies that the polarity of nonsense mutants depends on the failure of translation as such and not on the sequence of the nonsense codons themselves.

How widespread is the use of rho in bacterial operons? At least one other operon, the lactose operon, contains rho-sensitive signals, for De Crombrugghe *et al.* find that low concentrations of rho seem to cause transcription to halt at the end of the operon; but high concentrations generate a small RNA product, sedimenting at about 12–14S, which is of the size expected to correspond to only the first one-third or so of the *z* gene, the first gene of the operon. The correspondence of this location with a peak in the gradient of polarity (a region in which polar mutants have less effect upon the expression of subsequent genes) suggests that termination does not result from rho action at a site which by chance resembles true terminator sequences; it seems likely that the action of rho *in vitro* reflects the organization of the *z* gene *in vivo*. One possible implication is that the *z* gene may in fact comprise two genes, not one as has previously been thought.

The immediate significance of rho-dependent termination within an operon is that this mechanism may explain the natural polarity of some operons, in which later genes direct synthesis of less protein than earlier genes. This might be achieved by utilizing signals at the ends of genes which have lower affinities for rho than those at the ends of genes; rho recognition signals may yet prove to be present at the ends of all genes in an operon. Another variation on this theme is to suppose that there might be different kinds of rho factor to recognize the different signals. Conditions in the cell may differ appreciably from those *in vivo* so that defining the function of the rho factor as a cellular control protein must demand the isolation of mutants in the termination protein. De Crombrugghe *et al.* say that their next experiments will be to test the intriguing speculation that rho-dependent termination may provide an alternative explanation for the polarity of nonsense mutants; perhaps internal rho-dependent termination sites are activated when translation ceases at a previous nonsense mutation. B. L.

Cell Cycle in *Xenopus*

BETWEEN the stages of early gastrula and late neurula profound changes take place in the *Xenopus* embryo; the cells undergo about three divisions, increasing seven to eight times in number, and differentiated tissues such as notochord, neural tube, muscle somites and gut become recognizable histologically. But what would happen, one may ask, if mitosis is inhibited at the early gastrula stage, so that there can be no increase in cell number? The results of this intriguing experiment are reported on page 55 of this issue of *Nature* by Jonathan Cooke, of the University of Sussex.

Rather surprisingly Cooke found that nothing very drastic does happen to the development of the embryo if cell division is totally and rapidly inhibited at the early gastrula stage, either with colcemid or mitomycin C. The late neurula has all the differentiated tissues and morphology of the normal embryo, but only about one eighth the number of cells, which are correspondingly larger.

By itself this result is interesting in that it suggests that cells in the embryo do not have to go through a fixed number of divisions or normal chromosomal replications before differentiating. It does not, however, exclude the possibility that cells have to traverse part of the normal cell cycle to be able to respond to a change in positional information, a suggestion which has come from work on the insect cuticle. To test this hypothesis, Cooke transplanted a dorsal lip organizer into an inhibited embryo. This operation resulted in a second site of ectodermal invagination and the development of a second neural tube and notochord. In this way host cells were committed to a completely different developmental fate even though they could not undergo cell division. Experiments are in progress to test whether DNA synthesis and abnormal chromosome replication are still taking place in the colcemid-inhibited cells, and whether these processes are absolutely required for morphogenesis and differentiation.

From a Correspondent