Nunberg, Schimke and colleagues report in the November PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. But the DNA sequence repeated 200 times appears to be far larger than would be required for just the DHFR gene. The researchers are now examining whether the surrounding DNA sequences, which must also be amplified, are active.

The researchers propose that the many copies of the DHFR gene arise from selection of cells with gene duplications. Duplication of genes would occur infrequently and randomly, but a cell with an extra DHFR gene would have the advantage in the presence of low concentrations of the drug. Once the gene has duplicated, a number of mechanisms, such as unequal chromosomal crossing over, could generate further amplification.

When the cells are removed from the drug environment, some retain the increased number of gene copies, but others revert to the drug-sensitive state. In the latter case, the number of gene copies varies among the cells, and, in the absence of the drug, the cells with fewest copies multiply most rapidly and eventually dominate the population.

As rationale for drug therapy, these results suggest the use of sufficient amounts of multiple drugs for only as long as necessary. If resistance develops, a second set of multiple drugs should be used. Schimke and colleagues conclude, "Our results suggest that the prolonged administration of a single drug in ever increasing concentrations, which is retained in the environment, is precisely that form of administration most likely to result in amplification of genes in a stable state, thereby imparting stable resistance."

. . . and the gene is spliced

Resistant cells, with 200 active copies of a gene, are excellent raw material for recombinant DNA experiments, especially if the gene codes for a product that can be easily detected in both mammalian and bacterial cells. A group of Stanford University scientists led by Robert T. Schimke and Stanley N. Cohen now announce that the enzyme dihydrofolate reductase (DHFR) has been transferred into bacterial cells. They claim that their work is the first to show that the product of a mammalian gene in a bacterium is biologically active — some of the bacteria with the mouse gene could grow in the presence of an antibiotic that inhibits growth of normal bacterial cells. Similar experiments had been done earlier with yeast genes (SN: 3/12/77, p. 165). Unlike the work with somatostatin and insulin (SN: 9/16/78, p. 195), the product is not attached to a bacterial protein. The researchers say that the tests used to identify those hormones, binding to specific antibody, are not sufficient to demonstrate that the hormone will function naturally. □

Oaxaca quake was 'trapped' after all

While University of Texas geophysicists bemoaned their lack of funds to instrument an area in southern Mexico where they had accurately forecast the large Nov. 29 earthquake (SN: 12/9/78, p. 404), a joint team from California Institute of Technology and the University of Mexico were gleefully analyzing the data they had managed to collect with hastily installed portable instruments and the tiniest of research budgets. Their results, reported last week in a special paper delivered at a meeting of the American Geophysical Union in San Francisco, indicate that their luck and daring have paid off: their instruments "trapped" not only the main quake, but its precursors and aftershocks as well.

"I'm still amazed," Caltech senior researcher Karen McNally told her colleagues in San Francisco. Last August, she said, she had been invited to lecture at the University of Mexico, where professor Lautaro Ponce then discussed with her the possibility of a joint seismological survey of the Oaxaca area. Newly acquired portable seismographs of the University of Mexico would be used if Caltech could supply logistical support, such as radios for use in the difficult jungle terrain. McNally and her six co-workers would also help design the experiment, based on their work with monitoring swarms of "microquakes" in Southern California.

Ironically, the sense of urgency attending this arrangement stemmed largely from the researchers' agreement with the previous forecast of the University of Texas group. The concept that "gaps" in seismicity of an area may indicate its ripeness for a major quake is still controversial and McNally says the analysis of Gary V. Latham and others at U.T. made the Oaxaca gap "look like one of the best substantiated."

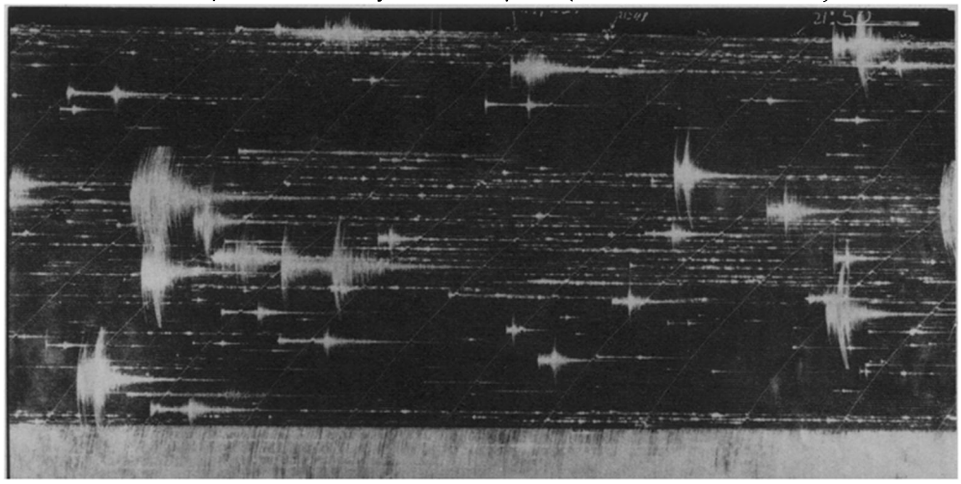
A key feature of that analysis was that a gap should show two distinct phases of activity before a major quake. In the "alpha" or quiescent phase, normal background seismic activity of small tremors should virtually cease as two plates of the earth's crust become locked along some region of the fault that marks their boundary. As the two plates continue to slip past each other, pressure builds up along the locked region until it reaches a breaking point. Just before the tension is released by slippage along the plate boundary that is felt as a major earthquake, a series of minor foreshocks may occur. The period of these small tremors, which may last for only days or weeks, constitutes the "beta" phase of gap activity.

Although more analysis of the new data will be necessary before any definite conclusions can be reached, McNally says her group may have measured the key transition between alpha and beta activity. When their instruments, sensitive to tremors as small as magnitude 1.0 on the Richter scale, were first installed at the beginning of November, little background activity was recorded. But during the two weeks just prior to the main 7.9 (approximate) magnitude quake on Nov. 29, shocks as large as magnitude 3.5 were recorded (see photo).

Such information, together with even more carefully measured aftershocks, makes up a "unique data set," McNally says. Perhaps only one other quake cycle, in Japan (SN: 4/29/78, p. 282), has been as thoroughly studied. The new data may help refine the seismicity gap model and perhaps provide information on the critical time factors involved, since the model now has no way to predict *when* an anticipated quake may occur.

The experiment also offers some lessons in international scientific cooperation and the occasional virtues of thinking small. The manager of grants and contracts for the Office of Earthquake Studies of the United States Geological Survey, Jack F. Evernden, told SCIENCE NEWS that the USGS had turned down the University of Texas application to study the Oaxaca area simply because they had asked for too much — several hundred thousand dollars. McNally asked USGS only for permission to divert $3,500 in existing funds to work on the joint project with the University of Mexico. The results of this work, McNally says, will first be submitted in condensed form to the American journal SCIENCE, then published in more detail in a Mexican journal. □

Series of foreshocks preceded the major Oaxaca quake (saturated area at bottom).



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