sumed during S phase[7,8]. In this model, the next round of replication in higher eukaryotes cannot occur until the nucleus has broken down, allowing the chromosomes to bind fresh licensing factor.

In budding yeast there is very good evidence for a licensing factor that controls, not DNA replication, but mating-type switching, an event whose cell-cycle regulation is similar to that of DNA replication. This licensing factor, the Swi5 protein, is made during G2 but is held in the cytoplasm because it is phosphorylated by Cdc28 (the budding yeast equivalent of Cdc2). At the end of mitosis, the inactivation of Cdc28 leads to the removal of the phosphate groups, allowing Swi5 to enter the nucleus, which like that of fission yeast has remained intact throughout mitosis[9]. Only when cells pass through Start is the Swi5 within the nucleus allowed to trigger the events that will lead to mating-type switching. Much weaker evidence supports the notion that a family of proteins, whose prototypic member is the budding yeast Cdc46 protein, act in a similar way to license DNA replication[10,11].

Could licensing factor in the nucleus regulate mitosis as well as DNA replication? In this model (*b* in the figure), the presence of licensing factor inside the nucleus prevents cells from entering mitosis. Like Swi5, licensing factor is made during G2, but phosphorylation by Cdc2 keeps it in the cytoplasm. The inactivation of Cdc2 at the end of mitosis allows licensing factor to enter the nucleus and keeps mitosis from occurring before the beginning of DNA replication. Because licensing factor is consumed during S phase and can only re-enter the nucleus at the end of mitosis, this scheme allows cells to pass Start only once between successive mitoses. In addition, it provides a simple explanation for the re-replication of DNA after the removal of Cdc2 from a G2 cell[6]. The loss of Cdc2 allows licensing factor to enter the nucleus at an inappropriate point in the cell cycle (see figure). As a result, when Cdc2 is resynthesized the licensing factor in the nucleus prevents the onset of mitosis, allowing another Start and S phase to occur.

In this view of events, Rum1 may act as an inhibitor of Cdc2 that is activated by the presence of licensing factor in the nucleus. A recent News and Views article[12] discusses a number of protein inhibitors of Cdc2 and related cyclin dependent kinases (Cdk), some of which preferentially inhibit particular Cdk–cyclin complexes[13,14]. In G1 the presence of licensing factor in the nucleus would activate Rum1, leading to a strong inhibition of Cdc2–mitotic-cyclin complexes that would prevent mitosis, and a weak inhibition of Cdc2–G1-cyclin complexes that would delay Start. Once licensing factor was consumed during DNA replication, the activity of Rum1 would decline, allowing the Cdc2–mitotic-cyclin complexes to drive entry into mitosis and exclude licensing factor from the nucleus. The overexpression of Rum1 would inhibit the activity of this form of Cdc2 thus preventing mitosis and allowing licensing factor to enter the nucleus, triggering a second round of DNA replication.

It remains to be seen which of these models for the function of Rum1 is correct. But elucidating the biochemical function of this protein promises to yield further insights into the regulation of DNA replication. □

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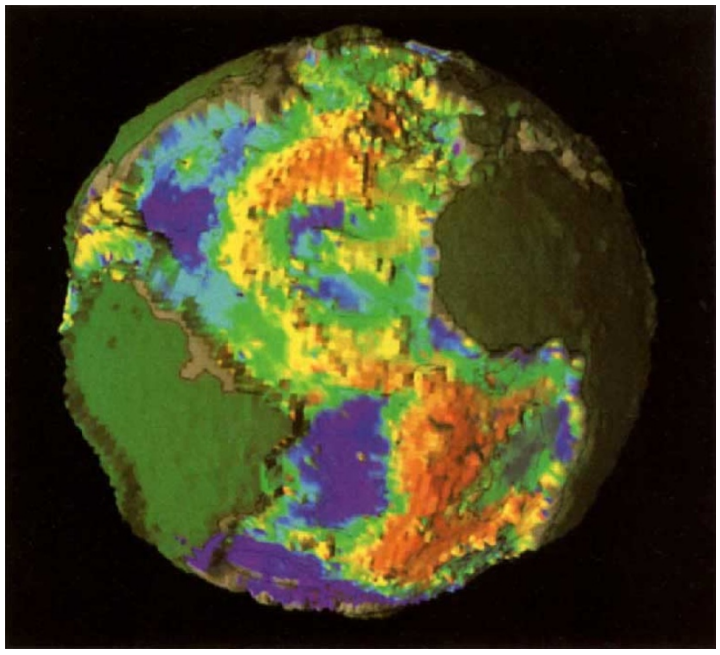
CARBON CYCLE

Compensation in the deep ocean



D. Archer

FOR calcium carbonate to dissolve in the oceans, pressure must be high, and the water must therefore be deep. In shallower regions, calcite is deposited on the sea bed, as shown in this computer simulation of calcite loading on and around the Mid-Atlantic Ridge. But the specific depth at which calcite first dissolves, and thus the area of the sea bed coated with calcite at any one time, depends on the total calcite concentration in a clever balancing act by the ocean. If the ocean receives more excess calcite via weathering, or some other source (such as changes in coral growth rates), carbonate chemistry works to increase the dissolution depth, so that more calcite can be deposited on the sea floor and buried by sediments to maintain a steady state.

On page 260 Archer and Maier-Reimer use this phenomenon to address the vexed question of why atmospheric carbon dioxide concentrations fell during the last glaciation. They point out that the atmospheric CO_2 concentration is controlled by ocean carbonate chemistry, and use a model that combines ocean circulation, carbon cycling and various sedimentary processes to try to test what sort of changes in calcite deposition would be required to account for the glacial change.

One suggestion that they test is the effect of a change in the relative deposition rates of organic carbon and calcite to the deep sea — organic carbon degradation in the sediments changes the pore-water chemistry, which in turn encourages calcite to dissolve and sets in train the whole compensatory mechanism. They find that decreasing the rate of calcite deposition by just 40 per cent relative to organic carbon deposition would be enough to account for the entire glacial CO_2 decrease.

Gabrielle Walker