overproduction of APP and/or reduction of lysosomal activity might accumulate the cytotoxic fragments within neurons, which eventually degenerate and die. In my view, 'extracellular' amyloid plaques could be harmless traces of dead neurons in the brain of Alzheimer's disease and related disorders.

Kazuaki Yoshikawa
Department of Molecular Neurobiology, Tokyo Metropolitan Institute for Neuroscience, 2–6 Musashidai, Fuchu, Tokyo 183, Japan

Cooling in the late Cenozoic

SIR — Raymo and Ruddiman in their Review Article[1] propose an explanation for the late Cenozoic climate cooling. Their approach, built from a comparison of data trends, is an inspired beginning. But it remains ultimately conceptual and primarily verbal, and thus omits an essential test of assembling a matter-conserving, dynamic numerical system. Because Raymo and Ruddiman contrast their concept (global weathering rate depends on rock supply) with opposing results drawn from a variety of quantitative models (global weathering depends on CO_2 supply), it is crucial that their hypothesis be subjected to similarly quantitative tests. Quantitative models of the carbonate–silicate geochemical cycle require an explicit system of equations for the fluxes of carbon to and from the ocean–atmosphere system and for atmospheric CO_2. I believe that if the authors were to place their hypothesis in the framework of a quantitative system model, major difficulties would appear.

Raymo and Ruddiman claim that uplift of the Tibetan plateau over the past 40 million years (Myr) provided a source of highly-weatherable silicate rock, which enhanced the rate of removal of atmospheric CO_2 to produce lower CO_2 and cooler climate. They recognize but do not satisfactorily answer the conundrum that an enhanced global weathering flux to the oceans requires an additional source of carbon dioxide to the atmosphere. Although they propose a lessening of carbon burial as one process (and potential others) that "would have partially counteracted a drawdown of atmospheric CO_2", a partial balance is nowhere near good enough. For example, were today's sinks of atmospheric CO_2 only 10% larger than the sources, CO_2 would be completely removed from the atmosphere–ocean system in a mere 5 Myr.

Perhaps Raymo and Ruddiman intend the net imbalance from the simultaneous, rather large perturbations of sources and sinks to be slight enough to weave reasonably-bounded CO_2 changes over 40 Myr? To my mind this would be threading an improbable needle. Although the time history of the Tibetan uplift is not available, Raymo and Ruddiman need to demonstrate that their concept in principle — using a model with explicit mass fluxes and reservoirs, and with numbers they cite, such as a 40% increase in weathering — does not lead to catastrophic drops in CO_2. I suspect that they will be forced to formulate some direct relation between atmospheric CO_2 and weathering, as used ubiquitously in the quantitative system models. Such models routinely produce outputs of temperature and isotopes for comparing to the geological record. I look forward to seeing actual numerical output produced by the Tibetan plateau hypothesis in the context of a dynamic system model.

Tyler Volk
Earth Systems Group, Department of Applied Science, New York University, New York, New York 10003, USA

SIR — Raymo and Ruddiman[1] propose a false dichotomy between climate hypotheses in which variations in atmospheric CO_2 are driven either by accelerated weathering accompanying tectonic uplift or by changes in CO_2 outgassing. Furthermore, they propose that mountain uplift is the primary control on the long-term global chemical weathering rate, and they discount the role of the CO_2 dependence of terrestrial silicate weathering as a major feedback control on atmospheric CO_2 content. We believe that their paper confuses a number of important issues.

Higher atmospheric pCO_2 may lead to higher temperatures, increased runoff, enhanced soil microbial activity and greater area coverage by vegetation at high latitudes, all tending to accelerate mineral dissolution rates. Hence, silicate rock should weather more easily when the atmospheric CO_2 concentration is higher. Because silicate weathering consumes CO_2, this would produce a negative feedback that could modulate long term atmospheric CO_2 content[2,3]. The calcium and magnesium released to rivers by the chemical weathering of silicate rocks, after entering the ocean and reacting with seafloor basalt, are predominantly buried as carbonates. Hence, on long timescales (>1 Myr), the chemical weathering of silicate rocks must roughly balance the flux of carbon available to be buried as carbonate. In the absence of variations in CO_2 outgassing and for a constant organic carbon subcycle, factors such as tectonic uplift, if it allows silicate rocks to weather more easily, would tend to decrease atmospheric pCO_2 without having any long-term effect on the global chemical weathering rate. To increase the long-term rate, an additional source of carbon is required.

Raymo and Ruddiman propose that the primary source of additional carbon leading to enhanced weathering rates in the mid-to-late Cenozoic is diminished organic carbon burial, which is equivalent to net organic carbon oxidation. (Contrary to Raymo and Ruddiman's characterization, the use of organic burial in carbon cycle modelling is not new[4–7].) However, the timing of changes in the Cenozoic carbon isotope record[8] do not closely correspond to changes in the strontium isotopic record. If terrestrial silicate-weathering rates were to have steadily increased by 40% over the past 40 Myr as proposed by Raymo and Ruddiman, then the net oxidation of this amount of organic carbon would require that O_2 levels were about twice as great as today 40 Myr ago. There is no independent evidence for this extreme situation. Enhanced burial of sedimentary pyrite is the primary possible non-atmospheric source of O_2 for net organic carbon oxidation. However, sulphur isotopic evidence points to little change and possibly some decrease in late Cenozoic pyrite burial rates[9,10].

The isotope evidence that Raymo and Ruddiman cite could be explained by processes they did not consider. For example, the carbon isotope signal after 15 Myr may not only reflect diminished organic carbon burial, but rather could be partly a consequence of diminished biological carbon isotopic fractionation[11,12]. (If the late Cenozoic trend has been towards lower pCO_2, then plants from later in this period should show less selectivity towards lighter carbon isotopes than did plants from earlier.) Also, the mid-to-late Cenozoic strontium isotope signal could be the result of the liberation of radiogenic strontium from old silicates during collisional orogenesis[13], rather than from an increase in overall weathering rates.

Organic matter burial cannot act as the feedback on atmospheric pCO_2 because factors other than atmospheric pCO_2 (for example, nutrient supply to the oceans) control the rate of organic matter burial[14]. The other two possible feedbacks suggested by Raymo and Ruddiman also have serious deficiencies. First, there is more evidence for authigenic calcium silicate formation in marine environments before 40 Myr ago than over the past 40 Myr (ref. 15), indicating that enhanced weathering could not have been balanced by enhanced authigenic calcium silicate formation in the late Cenozoic. Second, cal-