

that is analogous to transcytosis, such as post-endocytotic sorting of membrane proteins into synaptic vesicles or polarized axonal transport<sup>11</sup>. It is conceivable that alteration of APP processing coupled with augmented  $\beta$ -amyloid deposition during the early stages of Alzheimer's disease (at least in those cases bearing an APP structural mutation) could perturb a cascade of normal sorting functions, leading to disturbance of neuronal membrane architecture and turnover. Under such conditions, it is not hard to imagine that proteolysis of APP and formation and deposition of the  $\beta$ -amyloid fragment might increase, eventually leading to irreversible neuronal damage. Rethinking the context in which  $G_o$  might function could also resolve some of the controversies surrounding interactions of trimeric G proteins with proteins other than seven-transmembrane-segment surface receptors (for example, whether IGF-II receptor can signal or is only a transporter).

To address some of these issues, it will be necessary to examine the co-precipitation of APP not only with  $G_o$  but with other G proteins, GAP-43 and additional neuronal polypeptides, especially those associated with growth-cone membranes. The precedent of tyrosine kinase membrane receptors argues that functional complexes of membrane proteins may be elaborate<sup>13</sup>, and that many components involved in membrane traffic or transduction may form a dynamic unit. Another issue will be whether  $G_o$  might be involved in different types of neuronal injury or degeneration. If so, one crucial experiment will be to examine whether pertussis toxin is neuroprotective. In this respect, collapse of growth cones *in vitro* has been reported to require trimeric G proteins inactivated by treatment with pertussis toxin<sup>14</sup>.

The finding of an interaction *in vitro* between APP and a G protein opens up fresh prospects for research. But even if this process operates in intact cells, it

may relate more to the normal function and processing of APP than to its involvement in Alzheimer's disease. Several non-neural amyloid diseases involving other amyloidogenic proteins are characterized by the progressive deposition of a mutant and/or cleaved form of a normal polypeptide as amyloid fibrils, without necessarily perturbing the normal function of the parent protein. It remains to be seen whether increased formation and accumulation of the  $\beta$ -amyloid fragment, which is itself a nor-

mal product of cellular metabolism<sup>15-17</sup>, is accompanied by a phenotypically important change in the function of APP. □

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## ARCHAEOLOGY

# No Eden in the New World

Karl W. Butzer

WHAT was the state of the environment when the Spaniards arrived in the New World in the sixteenth century? And what effect did they have upon that environment? Three assumptions have insinuated themselves into the public

between autochthonous, biogenic lake sediments and the organic matter, soluble material or unweathered minerals derived from the leaching and erosion of soils in the catchment area and deposited within the lake. These core profiles are

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Cortés meets Montezuma in Mexico (circa 1519) — were the imported Spanish farming methods any more destructive than those of the native Americans?

consciousness — that prehispanic agriculture was environmentally benign; that Spanish colonial forms of land-use, especially stock-raising, were highly destructive; and that, more generally, traditional farming systems are inherently conservationist and point to ways in which to reduce environmental degradation today.

On page 48 of this issue<sup>1</sup>, O'Hara and colleagues provide convincing evidence for one centre of Mesoamerican civilization, around Lake Pátzcuaro in Mexico, that runs directly counter to these assumptions. They provide data from 21 cores that allow distinction to be made

dated and their microstratigraphy cross-correlated by 18 carbon-14 dates, primarily on charcoal and ostracodes; of these, 12 were measured by accelerator mass spectrometry to provide a remarkably consistent age framework of 4,000 years for the six lithological units identified, and one that is consistent with assumed dates for the regional archaeological sequence. This is a compellingly broad and accurate analytical database, far finer-grained than traditional pollen profiles. Moreover, unlike the more common, isolated limnological probes, it offers a three-dimensional picture of a catchment area and its

changing soil landscape over time.

The principal results are these. That there was an initial period of minor soil disturbance in the basin between about 1900 and 1250 BC (calibrated), coincident with the appearance of maize pollen. That a second, more intense episode of erosion occurred from about 600 BC to AD 650, linked to late Preclassic/early Classic occupation and concentrated in the northern part of the basin. And that a third, particularly destructive interval of soil erosion took place after AD 1200; this was initially centred on the Post-classic Tarascan (Purépecha) centre of Tzintzuntzan, and was followed by a slight decline in topsoil removal and a modest increase of mineral soil erosion after about 1500, during the Spanish and Mexican periods. Rates of soil-derived

sedimentation averaged 10,300 tons a year before about AD 650, 29,000 tons a year after about AD 1200, and 4,500 tons a year between these dates.

These figures show vividly that prehispanic indigenous land-use was not conservationist in practice. The curves suggest that an immediate response to reoccupation of the basin was an initial flush of topsoil, followed by a rapid, steady increase in mobilization of mineral sediment. Preclassic/Classic doubling of sedimentation rates implies that disturbance of the basin was then relatively modest, but Postclassic settlement provoked a sixfold increase and probably was environmentally destructive. The full scope of disturbance is barely hinted at in the coarse-grained pollen record from the basin<sup>2</sup>, which does not support the impli-

cit notion of a deforested catchment. 'Shifting' hillslope farming, with fairly substantial fallow periods, today favours an irregular cover of secondary woodland in those humid parts of Mexico with indigenous-style farming, more consonant with the persistent oak and other deciduous, arboreal pollen represented in the palynological record.

A small Spanish town was founded at Pátzcuaro in 1537, but Spanish agricultural settlement was concentrated beyond the catchment, in Morelia; local Spanish land-use was probably limited to initial, mobile cattle-raising, soon followed by winter pasturing of sheep from drier parts of the plateau. Traditional, indigenous land-use persisted around the lake, despite a steadily declining Tarascan population; but the new bishop intro-

OBITUARY

## Robert W. Holley (1922–1993)

IN a remarkable decade from the mid-1950s to the mid-1960s, a series of discoveries established the foundation of our understanding of how genetic information is expressed in living systems. Robert W. Holley, one of the major figures of this period, died of lung cancer on 11 February at Los Gatos, California, north of the Salk Institute where he had been a resident Fellow for the past 25 years. Holley's principal contribution was in isolating and determining the nucleotide sequence of the first transfer RNA, so providing enormous insight into one of the fundamental events in protein synthesis.

His work started in 1956, on a sabbatical that he took at the California Institute of Technology from Cornell University, when he carried out experiments designed to detect the acceptor of activated amino acids. It was in the mid-1950s that Francis Crick proposed the 'adaptor hypothesis', that a small nucleic acid molecule might act as an adaptor for aligning amino acids along a ribonucleic acid chain during protein synthesis. During this period Mahlon Hoagland, Paul Zamecnik and others showed that radioactive amino acids became bound to a low-molecular-weight RNA, later called transfer RNA. It quickly became apparent that there were at least 20 classes of transfer RNA molecule, each capable of accepting an individual amino acid. To understand the process fully, it became necessary to isolate an individual species and then to determine its nucleotide sequence.

Holley's background made him well-suited to tackle this task. He had received a PhD in organic chemistry at Cornell in 1947, following his undergraduate training at the University of Illinois. He taught

organic chemistry and also worked in a laboratory of the US Department of Agriculture at Cornell. He selected the method of counter-current distribution, and developed it to the point where it



Robert Holley in 1968, the year he gained the Nobel prize.

could separate individual transfer RNA molecules which were assayed by their ability to accept a specific amino acid. Starting in 1958, it took three years of hard labour to isolate a purified species of the alanine acceptor transfer RNA from yeast. He began with 140 kg of commercial yeast and extracted 200 gm of transfer RNA which yielded 1 gm of the purified alanine species.

During the next four years, Holley developed methods that made it possible to determine the nucleotide sequence of this purified species. He introduced many innovations in that work, and the sequence was determined by using two sequence-specific ribonucleases which broke the molecule into smaller fragments that could be sequenced. Partial digests allowed him to obtain larger fragments which ultimately led to the sequence of the entire molecule. In the age of the Human Genome Project, in which we talk about kilobases of nucleotide sequence, it is important to realize

that Holley's effort represented the beginning of this process, albeit in the much more difficult world of RNA sequencing.

He was very interested in the secondary and tertiary structure of the alanine transfer RNA. Out of his work came the well-known clover-leaf secondary structure with the anticodon bases in one loop. Virtually all transfer RNAs sequenced subsequently have this clover-leaf arrangement; its full significance was realized in 1973, in X-ray diffraction studies that revealed the backbone folding of yeast phenylalanine transfer RNA, which produces an L-shaped structure with the anti-codon at one end and the amino-acid acceptor at the other end, more than 70 ångströms away.

Holley's elucidation of the nucleotide sequence of the transfer RNA molecule occurred in the same period during which the genetic code was being deciphered, and he shared the 1968 Nobel prize with Marshall Nirenberg and H. Gobind Khorana, who played major roles in deciphering the code. He moved to the Salk Institute in 1968, where he worked productively on factors that stimulate growth in mammalian cells.

Robert Holley was a modest man with a quiet and warm personality, an avid interest in science and a keen appreciation of the thrill of scientific discovery. As a hobby, he worked as a sculptor, and those who have seen his elegant bronze statues realize that he could have had another calling, had he elected not to go into science. Alexander Rich

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duced Spanish technology here early on, probably including ploughs<sup>3,4</sup>. Most notably, the limnological record does not support the idea of an increase in environmental degradation, even after the 1700s when both Hispanic and indigenous populations expanded rapidly. This evidence finds further support in the parallel pollen record from the adjacent catchment of former Lake Zacapu, once the site of a livestock hacienda<sup>5</sup>.

O'Hara *et al.* have provided a landmark study which shatters the myth of precolumbian America as an Eden in which people were "transparent in the landscape"<sup>6</sup>. Native Americans were populous and technologically skilled. The sustenance of those populations required agriculture and a vigorous use of resources that could be as damaging as any pre-industrial land-use in the Old World, as the record from Lake Pátzcuaro now reveals. Spanish forms of land-use were evidently no more harmful to the environment.

The implications of this conclusion are considerable, for there is a claim, increasingly heard, that indigenous agriculture was operated as a sustainable system in harmony with nature, suggesting an ideal norm for the future<sup>7</sup>. That is an oversimplistic view which ignores the points that the introduction of European livestock has greatly reduced the risk of starvation among rural peoples, has improved nutritional balance, and has provided ready fertilizer for small farmers in marginal agricultural areas<sup>8</sup>. Small-scale, traditional agriculture can, ideally, be adapted to local conditions and may deliver sustainable yields with minimal capital investment<sup>9</sup>; it is certainly preferable to 'technodevelopment'. But it would be inadvisable to consider it a total panacea, rather than as a source of information to be drawn upon in selecting more beneficial agricultural practices and strains of crops<sup>10</sup>. □

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## Succeeding in the sand dunes

M. J. Crawley

ON page 53 of this issue<sup>1</sup>, Van der Putten and colleagues describe a neat piece of work on the succession of plant species in sand dunes. They show that there is asymmetry in the effect of soil pathogens on plants earlier and later in the succession, and that this effect may in part drive the process of the replacement of one species by another. The

exhibiting deterministic events akin to birth, growth, maturity, senescence and death, and as a process in which facilitation of one species by its predecessor was a vital component. At the other extreme were the disciples of Gleason's<sup>3</sup> individualistic concept of vegetation, who saw plant communities as mere accidents, as random assemblages from



W. H. Van der Putten

First colonist — a healthy stand of marram grass on virgin sand dune.

idea is at once enticing and contentious.

Succession is one of the few topics in ecology where the practitioners are disposed to make confident predictions. Species replace one another in a characteristic sequence (shade-tolerators replacing light-demanders, for instance), as each species progressively alters the environment so that conditions become conducive to the recruitment of their successor and hostile to self-replacement. Left alone for long enough, the ecosystem is supposed to progress serenely towards the climax vegetation appropriate to the local conditions of soil and climate. The very word 'succession' conjures up an almost regal orderliness in guiding a sequence of predestined dominants.

Where there has been controversy about plant succession<sup>2–5</sup>, it has been to do with the mechanisms responsible for the demise of the current dominant, and the extent to which species that occur early in succession facilitate the establishment of the later arrivals. At one extreme, Clements<sup>2</sup> saw successions as analogous to individual organisms,

the pool of species capable of existing under the prevailing conditions whose structure (such as it was) reflected little more than the vagaries of plant dispersal. In such communities, the principal mechanism affecting successional change was inhibition; once a species became established it simply stayed put, perhaps for a very long time. It monopolized the space and precluded the establishment of other, later successional species. Possession was nine-tenths of the law.

If inhibition is the main process determining the rate and direction of successional change<sup>6</sup>, what are the factors reducing the competitive ability of a dominant to the point that it becomes susceptible to invasion by its successor? Van der Putten *et al.*<sup>1</sup> provide an innovative experimental test of the hypothesis that species-specific soil pathogens can provide just such a mechanism. The authors chose to work on sand dunes, where the simplicity of the foredune succession allows one to assume that contemporary zonation in space reflects the succession of dominant species through time. The dune is built around