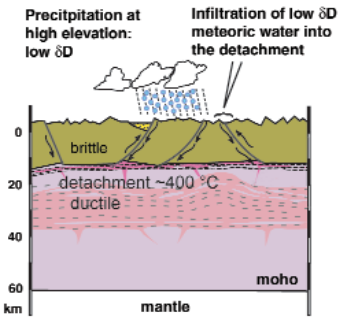
EDITORS' CHOICE

edited by Gilbert Chin

GEOLOGY

A High Water Mark

Many areas of the western United States and Canada harbor evidence of large amounts of a roughly east-west extension of the crust. It appears that during the past 50 million years, the crust seems to have been pulled apart along enigmatic shallow faults. In some areas, it is thought that the crust has been extended by much more than 50%, even though many of the extended areas are expressed as mountains today. One idea for the cause of this extension is that many of these regions represent even higher mountains or plateaus that subsequently collapsed.



A model of surface-derived water in an extensional detachment system.

Mulch *et al.* examined hydrogen isotopes in a hydrogen-bearing mineral, mica, that formed during extension in the Shuswap Complex in southwestern Canada. Hydrogen isotopes in part reflect elevation in precipitation, and the micas can be dated directly to the time of extension. The data imply that the Shuswap Complex once stood on average more than 4 km above sea level at the inception of its collapse, 45 to 50 million years ago, which is more than 1 km above its current elevation. Such high elevations may have characterized more of the western Cordillera at this time. — BH

Geology **32**, 525 (2004)

PHYSICS

Changing Constants?

Students of physics are taught that the fundamental constants of physics remain, well, constant with respect to time. That is, the laws of physics—the strengths of fundamental interactions—cannot be adjusted simply to accommodate observations that are not consistent with these laws. However, measurements of heavy-element isotope ratios that span geological time scales (billions of years) have indicated that the strength of the electroweak interaction, which is the force responsible for holding nuclei and electrons together and for radioactive beta decay, has, in fact, changed ever so slightly over this period.

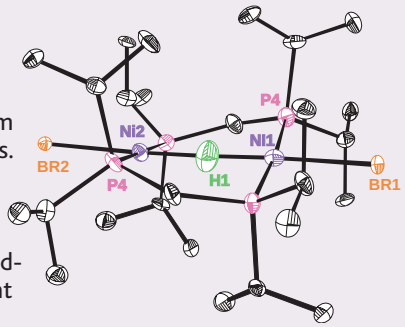
Researchers are conducting laboratory-based metrology experiments in order to ascertain whether the constants are changing and, if so, what the limits of these changes are. Fischer *et al.* have performed precision measurements of the 1S – 2S transition frequency in hydrogen and have found that if the fine structure constant does change with time, then it drifts by no more than 0.9 ± 2.9 parts in 1015 per year. Comparable precision measurements looking at the ratio of magnetic moments of cesium and rubidium atoms show that any drift in the ratio is limited to less than –0.5 ± 1.7 parts in 1015 per year. Although these are small numbers, absolute confirmation that the constants drift in value over time would have important implications for any theories that propose to bring together general relativity and quantum mechanics. — ISO

Phys. Rev. Lett. **92**, 230802 (2004).

CHEMISTRY

Kept in Line

In some bimetallic complexes, a single hydrogen atom bridges the two metal atoms via metal-hydride bonds. For one of the simpler examples of these compounds, $[HCr_2(CO)_{10}]^-$, structural studies at first suggested that the M–H–M geometry was linear with $D4_h$ symmetry, but subsequent neutron-scattering studies showed that the chromium complex adopted a bent geometry with a disordered hydrogen atom.



The nearly collinear halide (red), metal (blue), and hydrogen (green) atoms.

Vivic *et al.* describe a metal hydride complex for which neutron scattering reveals a nearly linear M–H–M angle (177.9°). The reaction of (dippm)$NiBr_2$, where dippm is bis(di-isopropylphosphino)methane, with two equivalents of 1-adamantylzinc bromide yielded a dark green solid with the terminal halide ligands in line with the nickel-hydride bonds. Initial studies of the compound's reactivity show that the dippm ligand is highly susceptible to reaction with basic reagents. — PDS

J. Am. Chem. Soc. 10.1021/ja047956k (2004).

BIOMEDICINE

Morphing into Metastasis

Epithelial-mesenchymal transitions (EMTs) are processes in which normally immotile epithelial cells are converted into cells that are capable of migrating. Long recognized as a critical step in the tissue remodeling that occurs during animal embryogenesis, EMTs have more recently been implicated in tumor progression and metastasis, events that likewise involve tissue remodeling and cell migration.

Exciting new evidence illustrating the importance of EMTs in tumorigenesis is provided by Yang *et al.*, who report that a transcriptional regulator of embryonic morphogenesis called Twist is required for tumor metastasis in a mouse model of breast cancer. Overexpression of Twist caused tumor epithelial cells to lose their adherent properties, become motile, and express markers of mesenchymal cells: all characteristic features of EMTs. Conversely, suppression of Twist expression by RNA interference produced a marked decline in the numbers of circulating tumor cells and lung metastases in the mice. In support of the clinical relevance of these observations, Twist expression levels in human breast cancer specimens were found to be highest in the most invasive tumors. Further studies of the mechanisms driving EMTs may help identify new drug targets for cancer. — PAK

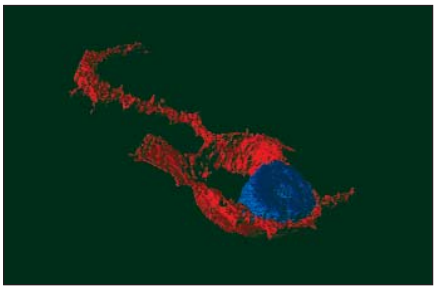
Cell **117**, 927 (2004).

CONTINUED ON PAGE 21

VIROLOGY

Of Mice and Men

An enigma of HIV biology has been the inability of infected rodent cells to support virus replication—meaning the production of correctly assembled viral particles. The viral gag-pol messenger RNA (mRNA) uses the viral protein Rev (which binds to the Rev response element within the mRNA) to bind to the nuclear export factor Crm1, but even though the mRNA is translated into Gag in the cytosol, the resulting protein is not properly localized to the plasma membrane, a step preparatory to the assembly and budding of mature viral particles. By shunting the viral mRNA into the export pathway mediated by the constitutive transport element–NXF1 interaction, Swanson *et al.* succeed in demonstrating HIV assembly in mouse cells. How the nuclear export of mRNA dictates where (and perhaps in what context) cytosolic translation occurs is unclear, but this finding may help both to establish a rodent model system for studying HIV and to understand the future consequences of early-life marks. — SMH



Gag protein (red) arrives at the cell periphery when exported from the nucleus (blue) via an alternative pathway.

CREDIT: SWANSON *ET AL.*, *EMBO J.* 10.1038/SJ.EMBOJ.7600270 (2004)

EMBO J. 10.1038/sj.emboj.7600270 (2004).

IMMUNOLOGY

Under the Influence

Autoimmune diseases such as type 1 diabetes are thought to occur, in part, because of a breakdown in the normal regulatory networks that operate among T cells. Although our understanding of regulatory T cell function is improving, how potentially autoaggressive T cells might be rendered responsive to this regulation is not completely clear.

Using a mouse model of type 1 diabetes, McGregor *et al.* examined the role of CD154 and its receptor CD40: a well-characterized pathway in T cell activation. Although transgenic coexpression of the inflammatory cytokine tumor necrosis factor and the T cell activation ligand CD80 in pancreatic islet cells rendered these mice susceptible to diabetes, onset of the disease was significantly hastened in the absence of CD154. This corresponded with a decline in the presence of T cells with a regulatory phenotype, as well as an impaired ability of disease-causing T cells to respond to regulatory signals. Indirectly, this suggests that the CD40 ligand expressed by autoaggressive T cells is required to sanction the acceptance of regulatory cues. — SJS

Proc. Natl. Acad. Sci. U.S.A. **101**, 9345 (2004).

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Genetic Variation in Alcohol Tolerance

The nematode *Caenorhabditis elegans* exhibits a decline in locomotor activity as an acute response to ethanol. In the continued presence of ethanol, the strains N2 and CB4856 show slow and rapid recovery (albeit incomplete) of movement, respectively. Through genetic analysis, Davies *et al.* map the differences in this rate of adaptation to ethanol to *npr-1*, a gene that encodes a homolog to the mammalian neuropeptide Y (NPY) receptor. The CB4856 allele of *npr-1* is lower-functioning than that of N2, and the authors propose that NPR-1 exerts an inhibitory influence on the development of tolerance. Interestingly, these alleles of *npr-1* are known to account for differences in behavior (N2 are solitary, while CB4856 are more sociable), yet the social behavior roles of NPR-1 and the ethanol tolerance effect were separable based on genetic interactions and targeted expression studies. NPY signaling has been implicated in alcohol responsiveness in mammals, and further investigation with the genetically tractable nematode may lead to additional insight into the molecular mechanisms that contribute to alcoholism. — NG

Neuron **42**, 731 (2004).