

breakup would not directly explain its origin — India did not split from the Seychelles until 65 million years later. However, the apparent isolation of Biju and Bossuyt's frog family in India supports the biotic ferry model. Molecular-clock studies of other living groups of plants⁹ and animals^{10,11}, including caecilians (limbless amphibians), also indicate that India developed a unique biota during its northward trek.

But why does the current biota reflect such isolation while the late Mesozoic fossils of India indicate past land connections ('biotic bridges')? Perhaps those bridges were more like chains of islands that allowed some — but not all — groups to disperse, as occurred in the past history of plant and animal interchange between North and South America¹².

The discovery of this remarkable new species adds to growing evidence of past isolation in the biogeographical history of India. Nonetheless, it is unclear why India's Mesozoic partner Madagascar lacks some major groups of vertebrates, such as caecilians and representatives of the new frog family, when evolutionary analyses indicate

that they should have been there in the past. Clearly, there is a need for more fossil collections and investigation of living faunas, and for refined molecular clocks, to better understand how continental drift influenced India's biota.

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Earthquakes

Good tidings

Christopher H. Scholz

Tidal stresses in the Earth's crust don't seem to influence earthquakes. Water wells, on the other hand, seem strangely sensitive to seismic activity. Explanations are now proposed.

The respective absence and presence of two phenomena associated with earthquakes has been puzzling geophysicists for more than a century. One is the general lack of correlation between earthquakes produced by tectonic forces and the 'solid Earth tides', which are caused by the oscillating stresses created in Earth's crust by the gravitational forces exerted by the Sun and the Moon. The other is that some water wells are extraordinarily sensitive to the seismic waves of distant earthquakes. Papers by Beeler and Lockner¹ and by Brodsky et al.², both in the *Journal of Geophysical Research*, help to explain these phenomena — and perhaps a few others as well.

If earthquakes have simple behaviour, in which stress on a fault builds up to some threshold at which the fault fails, then one would expect their occurrence to correlate with the daily Earth tides. After many increasingly sophisticated studies, no such general correlation has been found. Yet it has been recently recognized that changes in 'static stress' from earthquakes can trigger other earthquakes³, even when the stress change is as low as 1 kilopascal (ref. 4) — which is roughly the same mag-

nitude of effect associated with Earth tides.

Beeler and Lockner¹ conducted rock friction experiments in the laboratory to simulate the situation of a small sinusoidal loading (the Earth tide) being superimposed on linear loading (a fault being loaded tectonically). The laboratory equivalent of the earthquake cycle is 'stick-slip' events, in which frictional stress builds up at a 'fault' until its adjacent sides begin to slip and a slip instability occurs (Fig. 1a). Beeler and Lockner mapped the amplitude of the oscillating stress necessary to produce correlation with stick-slip events as a function of the oscillation period. They found two regimes. For oscillations with periods greater than a critical time, the correlation amplitude decreases as $1/f$, where f is the frequency of the oscillation. This is just as would be expected from a model — the Coulomb threshold model — which assumes that failure occurs at the peak stress. At periods shorter than the critical time, they found that the correlation amplitudes become frequency independent and are orders of magnitude larger than expected from the Coulomb model (Fig. 1b).

The key point is that the stick-slip instability in rock friction is not abrupt. Rather, it

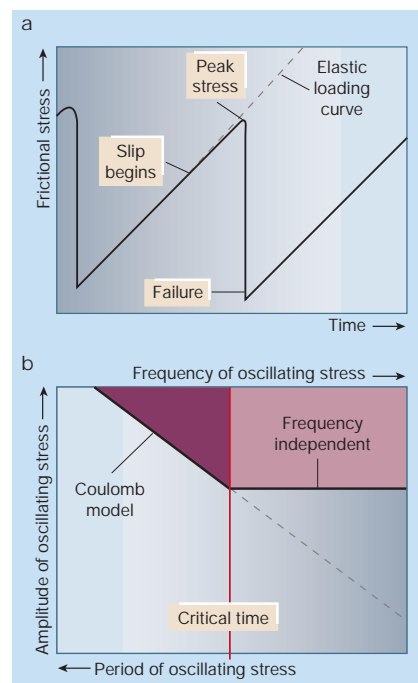


Figure 1 **Stick-slip and Earth tides.** a, The stick-slip process describes the changing level of frictional stress at a fault over time. Adjacent sides of the fault stick together as frictional stress builds up, but then begin to slip as the rate of stress change starts to diverge from the elastic loading curve. The peak stress value is reached slightly ahead of the point of failure. b, Beeler and Lockner¹ looked at the amplitude of oscillating stress, mimicking Earth tides, that reproduces stick-slip events. For oscillations with periods greater than a critical time, the correlation amplitude follows the Coulomb threshold, decreasing in inverse proportion to the oscillation frequency (all scales are logarithmic in this plot). But for short-period, high-frequency oscillations, the threshold for correlation no longer changes with frequency, and is considerably higher than would be expected in the Coulomb model.

follows a nucleation phase, in which the rate of slip increases as an inverse power law of the time to failure, leading to a peak in stress. Fault failure occurs following the peak. The critical time dividing the two correlation regimes corresponds to the duration of nucleation, which is inversely proportional to the linear stressing rate. This nucleation requires that frictional resistance increases with slip velocity and decreases with slip displacement. Beeler and Lockner have constructed a friction law incorporating these properties — a simple form of rate-state variable friction⁵ — and show that it correctly predicts the behaviour in the high-frequency regime.

At periods greater than the nucleation time, the nucleation has no effect. But at shorter periods it greatly dampens the triggering effect, so that much higher amplitudes

are required to produce a correlation. For instance, given the stressing rate on the San Andreas fault, the nucleation time exceeds a year. So a static-stress change of the same amplitude as Earth tides can trigger earthquakes. But the tides are well into the high-frequency regime and are far too low in amplitude to do so.

In their work, Brodsky *et al.*² studied the response to earthquakes of a well in Oregon. The well is set in granite, and amplifies the long-period seismic waves produced in earthquakes by a factor of about 300: a long, thin crack intersects the borehole at depth and acts as a bellows, drawing water in and out of the well when compressed and expanded by seismic waves. Curiously, however, the surface waves of large earthquakes as much as 3,000 km distant produce sustained changes in water level of about 10 cm.

Brodsky and her colleagues put forward a model in which groundwater flow through the crack deposits weathering material that clogs the crack. They propose that the passage of surface waves dislodges the blockage, allowing the pressure in the crack to re-equilibrate, resulting in a step in water level in the well. Two independent corroborations make this a convincing argument. Brodsky *et al.* observed that the amplification factor of the well increased by several orders of magnitude during a step, suggesting that the length of crack in communication with the well had greatly increased during the step. Furthermore, although the 1999 Oaxaca earthquake in Mexico (magnitude 7.4) produced an 11-cm step, the Hector Mine earthquake in California (magnitude 7.1), which followed it 15 days later, did not. The implication is that insufficient time had passed to form a new blockage.

The same physics embodied in Beeler and Lockner's analysis¹ with Earth tides explains why dynamic triggering by seismic waves requires much greater stress amplitudes (1–10 megapascals) than does static triggering⁶. As a result, static triggering dominates and dynamic triggering can be distinguished only under special circumstances⁷. The exception is volcanic areas, where earthquakes occur through the stress effects produced by magma activity on fractures in the rock. In this case, surface waves, similar in amplitude to those that produced steps in the Oregon well, can trigger earthquakes at large distances⁸. Brodsky *et al.* suggest that the unclogging mechanism may be responsible for that phenomenon also, because such steps would result in static-stress changes.

Earthquakes in volcanic regions differ from tectonic earthquakes in another way: earthquake 'swarms' in such areas have often been found to correlate with Earth tides⁹. This could happen because the stressing rate during swarms is much greater than tectonic

rates, so that the nucleation time becomes less than the tidal period. This is implied by an analysis of dynamic triggering by seismic waves in a volcanic region, which shows a threshold that depends on $1/f$, the characteristic of the low-frequency regime¹⁰. Otherwise, perhaps some crack–fluid interaction, such as that found by Brodsky *et al.*², could be triggered by the tides. ■

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Proteomics

Where's Waldo in yeast?

James A. Wohlschlegel and John R. Yates

Research in yeast provides the tools and benchmarks for a wide sweep of biology. The latest results reveal the most complete picture yet of the levels and locations of protein production in the organism.

Biologists have just completed a round of 'Where's Waldo?' with proteins of the yeast *Saccharomyces cerevisiae*. 'Where's Waldo?' is a popular children's game that entails finding every figure of Waldo in an intricately drawn picture. In some areas of the picture, Waldo blends in well with the background and is difficult to find; in others he stands out. Two papers in this issue (pages 686 and 737)^{1,2} describe large-scale studies of the yeast proteome, which had the goals of quantifying the levels of every protein expressed in yeast cells and determining the subcellular compartment in which the protein resides.

Saccharomyces cerevisiae was the first eukaryote — the type of organism characterized by a nucleus and membrane-bound organelles, which also includes humans — to have its genome sequenced³. Work with this organism has since led the way in functional genomics. Experiments pioneered in yeast have set the standard for the global analysis of cellular processes and paved the way for similar approaches in other organisms. They have also generated genome-wide collections of reagents that have been tremendously valuable.

Open reading frames (ORFs) are commonly the centre of attention in genome biology. These are stretches of DNA that have the characteristics of protein-coding capacity; that is, they may be genes. Collections of yeast strains now exist in which the expected ORFs have been either deleted or fused to various protein tags^{4,5}. Arrays have been created by using yeast strains expressing proteins that carry so-called affinity tags, allowing large numbers of proteins to be rapidly purified, then immobilized on a solid support⁶. Large-scale studies involving various techniques — protein arrays, and yeast

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two-hybrid or co-immunoprecipitation assays — have revealed the identities of proteins that interact with individual proteins, large macromolecular complexes, or even specific small molecules^{7–10}.

All in all, yeast biologists have led the charge in developing approaches to understanding eukaryotic genomes. Huh *et al.*¹ and Ghaemmaghani *et al.*² continue that tradition. Their goal was to tag and study the gene products of all recognized ORFs in the yeast genome. A key component of these studies was the tagging method used: artificially altering a protein's expression level can lead to results, such as mislocalization, that do not reflect its characteristics when it is expressed normally.

In technical terms, Huh *et al.* and Ghaemmaghani *et al.* used homologous recombination to integrate a DNA sequence, encoding either a tandem affinity purification tag (TAP) or green fluorescent protein (GFP), in-frame with the 3'-end of the coding sequence of each gene in its original chromosomal location. Because a gene's promoter and upstream regulatory sequences are not affected in this approach, it is likely that the behaviour of these fusion genes is nearly identical to that of their normal counterparts.

Ghaemmaghani *et al.*² created a collection of yeast strains in which each annotated ORF was fused to a TAP tag. In turn, the tag was used to measure the absolute expression levels of each protein by a technique known as quantitative immunoblotting. They found that around 80% of the ORFs are expressed in growing yeast cells at levels ranging from 50 to 1,000,000 copies per cell. Knowing what portion of the yeast genome is expressed, and the absolute protein abundance, will help in verifying the accuracy and detection limits