proliferative potential of epidermal stem cells[8]. In the impressive accompanying clinical studies[9], the researchers obtained limbal stem cells from the healthy eye of 112 patients with ocular burns, cultivated them and then transplanted the cultured cells onto the patients' damaged eye. After an extensive 10-year monitoring period, the authors now report[1] permanent restoration of a transparent, self-renewing corneal epithelium in three-quarters of the study patients (Fig. 1c). Notably, 78% of the successful transplantations involved cultures in which p63-expressing cells constituted more than 3% of the cells capable of forming colonies. These observations unveil a direct correlation between the percentage of p63-positive corneal stem cells in a culture and their transplantability. The correlation presents a powerful diagnostic tool for predicting whether any given limbal culture is likely to be suitable for long-term transplantation.

This work[1] also offers hope for exploring alternative sources of limbal stem cells to treat patients who have suffered severe injuries to both eyes, and who therefore lack limbal stem cells. Indeed, in the future it might be possible to create corneal stem cells by culturing other cells from the patient — for instance, skin stem cells — and then either directly inducing their transdifferentiation to limbal cells, or transforming them first to an embryonic-stem-cell-like state (induced pluripotent stem cells, or iPS cells) before inducing their differentiation along the limbal lineage. To achieve such stem-cell therapies and improve on the existing ones, researchers will need to learn more about how corneal stem cells differ from their skin counterparts. Better protocols must be devised for purifying stem cells and for preserving and enhancing their self-renewal *in vitro*. And protocols for transdifferentiation and/or iPS-lineage differentiation will need to be established for the generation of limbal stem cells.

Pellegrini, De Luca and colleagues' work[1] elegantly demonstrates how the knowledge of one type of stem cell — in this case, the human epidermal stem cell — can be used to advance a clinical treatment for another, the limbal stem cell. Their paper sets the gold standard for the level of scientific proof that is needed for each new stem-cell therapy, and provides a blueprint that can be applied to the development of other adult stem cells for clinical therapies. Stem-cell therapy still has a long journey ahead, but the light is beginning to shine brightly on its path. ■

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EARTHQUAKES

Climate and intraplate shocks

Mark D. Zoback

The heartland of the United States lies within a tectonic plate, certain regions of which have experienced large and geologically recent earthquakes. Explanations for those events are still being sought.

Over the past several decades, the earthquake cycle along tectonic-plate boundaries has become increasingly well understood. There is a consensus that geological, geodetic and palaeoseismic data can be combined to establish long-term earthquake probabilities, with a degree of certainty that improves as more and better data become available.

There is no such consensus when it comes to intraplate earthquakes. The reason is that there are no well accepted principles that account for why large earthquakes have occurred where they did in the recent past, where they are likely to occur in the future, or how large they might be. In this context, Calais *et al.*[1] (page 608 of this issue) provide a valuable contribution. Their study region lies in the central United States, around New Madrid, Missouri, which in 1811–12 experienced a sequence of three earthquakes estimated to be of magnitude 7 or larger.

Much still needs to be done to reduce earthquake hazards for those living along active plate boundaries. To recognize that, one needs only to look at the devastating consequences of the 2004 earthquake and tsunami in Sumatra (230,000 dead in 14 countries), or the earthquake in Haiti earlier this year (approximately 200,000 dead and 2 million left homeless). But the situation is even worse in intraplate regions, especially in the developing world. In the past decade alone, tens of thousands of people have died in each of the earthquakes that hit Bhuj, India (2001), and Bam, Iran (2003), as well as in the magnitude 7.9 Wenchuan event that occurred in China in 2008 (Fig. 1). We know that intraplate earthquakes result from plate-driving forces transmitted through plate interiors[2,3]. But without a better understanding of why intraplate earthquakes occur where they do, the potential for future damaging earthquakes must be considered 'high impact but low probability'. In the developing world, it is unlikely that much will be done to prepare for such events.

The New Madrid seismic zone is the best studied of locations that have been affected by intraplate earthquakes. One of the enigmatic features of this zone is the rate at which large earthquakes occur. Palaeoseismic data[4] indicate the occurrence of at least three, and possibly five, large earthquakes (or sequences of such earthquakes) in just the past few thousand years. However, faults seen on seismic reflection profiles show little cumulative deformation over the past few million years[5], during which time the regional geological processes have been essentially identical. Hence, the long-term earthquake rate seems to be much lower than that of the past few thousand years.

Moreover, unlike at plate boundaries, where over time the average rate of seismic-strain release in big earthquakes matches the rate at which strain energy accumulates as a result of relative plate motion, analysis of data from the Global Positioning System (GPS) has shown that the rate of strain accumulation in the New Madrid region is quite low[6]. The occurrence of multiple large events in a relatively short period of time seems to be due to the release of strain energy that accumulated over a very long period of time.

In turning to the new paper by Calais *et al.*[1], I should declare an interest in that the model used is conceptually similar to one proposed by Grollimund and myself a few years ago[7]. Both studies invoke the consequences of the retreat of glaciers from much of continental North America at the end of the last ice age. And both assume that the brittle crust is in a state of frictional failure equilibrium — that is, even in relatively stable plate interiors, stress levels are close to that at which slip could occur on faults that are appropriately oriented to the current stress field. This allows even a relatively small perturbation of stresses in the lithosphere to induce brittle faulting in the upper crust, and time-dependent flow in the viscous lower crust and upper mantle.

In Calais and colleagues' model[1], the perturbation is caused by localized erosion of approximately 12 metres in the past 16,000 years, produced by river incision. This induces upward flexure of the lithosphere in the New Madrid area, 'unclamping' some of the critically stressed faults in the region. In our paper[7] we argued that, consequent on the removal of ice-sheet load, seismicity is localized around New Madrid because of anomalously low

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Figure 1 | Consequences of an intraplate earthquake. Yingxiu town, Wenchuan county, seen in the wake of the seismic events of 2008.

viscosity in the upper mantle, the result of an ancient, failed rift in the region.

Importantly, both models produce crustal deformation rates that are consistent with the rates observed by GPS measurements in the region; and both predict that the rate of large earthquakes seen over the past few thousand years is likely to continue for thousands of years into the future, because of the long time it takes for the triggered viscous flow in the lower crust and upper mantle to diminish. In other words, seismic hazard in the region remains high. The paper by Calais *et al.* is valuable both in reinforcing that point and in providing a plausible mechanism that merits further investigation.

It has been argued[8] that, as in the New Madrid region, several intraplate fault zones in Australia have exhibited episodes of relatively frequent earthquakes separated by long periods of quiescence. Similar behaviour may characterize earthquakes in the southeastern United States near Charleston, South Carolina[9]. These regions, as well as others that have been struck by intraplate earthquakes, deserve detailed study, with the aim of revealing what might have triggered the release of strain energy stored in Earth's crust for millions of years. ■

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OCEANOGRAPHY

Century of phytoplankton change

David A. Siegel and Bryan A. Franz

Phytoplankton biomass is a crucial measure of the health of ocean ecosystems. An impressive synthesis of the relevant data, stretching back to more than 100 years ago, provides a connection with climate change.

In 1865, Father Pietro Angelo Secchi was asked to map the clarity of the Mediterranean Sea for the Papal navy. He invented the simplest of oceanographic instruments: a 20-centimetre-wide white disk that is lowered until the observer loses sight of it, and for nearly 100 years determinations of Secchi depth were a routine part of oceanographic observations[1,2] (Fig. 1, overleaf). Secchi-depth determinations assess light penetration in the upper ocean, and can be related to phytoplankton abundance. Along with measurements of the upper-ocean concentration of chlorophyll, which is found in all phytoplankton, Secchi-disk depths provide the only data available for assessing changes in the global ocean biosphere over the past century.

Boyce *et al.*[3] (page 591 of this issue) have revisited those data, and have synthesized all available information to assess changes in phytoplankton biomass on decadal to centennial timescales, and over regional to global spatial scales. Taking great care, they created time series of phytoplankton biomass in the pelagic ocean, quantified as surface chlorophyll concentrations. They find a strong correspondence between this chlorophyll record and changes in both leading climate indices and ocean thermal conditions. They also show statistically significant long-term decreases in chlorophyll concentrations for eight of the ten ocean basins, and for the global aggregate.

Boyce and colleagues' findings are consistent with analyses of satellite observations of ocean colour, in which decreases in indices of phytoplankton productivity are mirrored by increases in ocean warming[4–6]. Satellite ocean-colour observations sample the entire globe within two days. In fact, in less than 30 seconds, the Sea-viewing Wide Field-of-view Sensor (SeaWiFS) makes nearly half a million independent observations — equivalent to the entire historical record synthesized by Boyce and colleagues. But high-quality, global satellite observations of the ocean biosphere have been available for little more than a decade — too short a time to quantify and understand the causes of long-term trends[7].

The analyses of Boyce *et al.* document the historical record. Looking into the future, however, satellite measurements will be the main source of data for assessing change in pelagic ecosystems. The principle is simple — the colour of the 'water-leaving' sunlight is used to determine chlorophyll concentrations. Turning that principle into practice is not simple.

First, satellites measure the reflected sunlight at the top of the atmosphere, and, typically, fewer than 10% of the photons detected relate to the oceans' water-leaving signal. Hence an atmospheric correction is required to quantify a much smaller ocean-colour signal[8]. Furthermore, the measurements must be accurate and stable enough to assess change over inter-annual timescales[9]. This requires both the on-orbit assessment of alterations in sensor characteristics over time, and a procedure to provide absolute sensor calibration[8–10]. Finally, a bio-optical model is needed to convert the remote assessments of ocean colour to oceanographically relevant quantities[11], along with field observations to validate the satellite results. Thus, many interdependent components are required to create satellite observations of ocean colour that will be useful in assessing the response of ocean ecosystems to climate change.

Another consideration is that satellite missions planned at present have lifespans of only about five years, so establishing a multi-decadal time series of observations requires data from several missions. Unlike the Secchi disk,

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