single tube, and its contents loaded onto a chip containing microwells that each accommodate only two droplets. The droplets distribute randomly into the microwells, to constitute what the authors refer to as a self-assembling array, such that each amplified nucleic-acid target is expected to be exposed to each detection mix, in multiple replicates in different locations on the chip. Exactly where this happens is revealed by recording the two colour codes present in each well.

The detection reactions are then initiated simultaneously in each well by merging the droplet pairs by exposure to an electric field. If an amplified viral sequence is in a well that contains Cas13 in complex with a guide RNA that can recognize this sequence, Cas13 is activated and its nonspecific RNA-cleavage activity generates a fluorescent signal from the reporter RNA. This platform is admirably innovative, marrying the desirable characteristics of the ability of the guide RNA–Cas13 complex to recognize a specific sequence with a labour-saving platform that is inherently flexible because the user can select the PCR reactions and the guide-RNA sequences used.

To illustrate the potential application of CARMEN for broad testing of virus samples, the authors show that the technique could simultaneously detect all 169 human viruses for which at least 10 genome sequences were available at the time. The authors also demonstrate that CARMEN enables comprehensive identification of different influenza strains from samples obtained from infected people. This is important, because it could allow detection of a newly emerging type of influenza. CARMEN can be adapted to detect a viral variant resulting from a mutation after the variant sequence is determined. Ackerman and colleagues report that, when CARMEN was used on samples from people infected with HIV, it could detect six known viral mutations associated with drug resistance.

Finally, the authors illustrate CARMEN's flexibility by rapidly adapting the system to detect SARS-CoV-2, the coronavirus that causes COVID-19. The authors report that CARMEN distinguishes SARS-CoV-2 from the other human coronaviruses, including four seasonal coronaviruses and the coronaviruses responsible, respectively, for severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Rapid, sensitive and specific detection of SARS-CoV-2 by a method using CRISPR and Cas12 has recently been reported[6], and that technique has similarities to CARMEN but only one type of virus can be detected.

How does CARMEN compare with other emerging diagnostic platforms? In the breadth of its detection, CARMEN is most similar to the microarray methods used for the simultaneous detection of amplified nucleic acid from multiple viruses[7]. But CARMEN has the advantage of avoiding the need to manufacture in advance microarrays that contain the specific nucleic-acid sequences needed.

Commercially available multiplex PCR panels, now widely used in diagnostics in clinical laboratories, provide another possible platform[8]. These kits, described as 'sample-in, answer-out' systems, are admirably simple to use and can detect 20 or more targets in just over an hour. However, they are not modifiable by users in the way that CARMEN is — the kits come preloaded with the components needed to amplify nucleic acids and have been optimized for a specific combination of targets.

Another option is metagenomic sequencing[9], which is a next-generation sequencing approach that directly determines the sequences of any nucleic acids present without needing a PCR-based amplification step or a specifically tailored reporter probe to detect particular sequences. However, compared with CARMEN, this method requires more-complex equipment and data processing, and takes longer to generate results.

Although CARMEN incorporates numerous desirable features for the surveillance of emerging infectious disease or the identification of a viral infection, there are some concerns. First is that the CARMEN workflow includes the manipulation of amplified nucleic acid, and so there is the risk of contamination. Perhaps appropriate automated instrumentation could reduce this key vulnerability. Second, will off-target effects of Cas13, possibly resulting from binding of guide RNAs to incorrect targets, lead to nonspecific detection reactions? Third, will the generation and image analysis of the nanodrops in these chips be sufficiently robust under 'field conditions' in a range of different types of laboratory, considering the need for sophisticated fluorescent-microscopy analysis, and given that users will have different levels of experience and expertise?

Finally, the sequences used to amplify RNA and the guide RNA sequences used might need to be changed to achieve optimal sensitivity and specificity and to account for virus variation over time. These issues need to be taken into account, but they do not lessen the authors' achievement in developing a new diagnostic platform designed around the need for surveillance of global emerging infectious diseases.

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Earth science

Force takes control in mountain-height debate

Kelin Wang

What controls the height of mountain ranges? An analysis of the forces acting on mountains near tectonic-plate boundaries suggests that tectonic forces are the main controller, rather than climate-driven erosion. **See p.225**

It is common knowledge that mountain ranges were created by tectonic forces, but how their height is maintained today is a matter of debate. A widely held view is that climate-controlled erosion limits their height[1,2]. On page 225, Dielforder *et al.*[3] take a different stance. They show that, at least for mountain ranges that are near convergent tectonic-plate boundaries, tectonic force has a dominant role in controlling height.

The mountain height discussed by the authors is that of a smoothed version of the actual mountain topography, in which high peaks and deep valleys are omitted. The natural processes that maintain this mountain height can be simplified into three types (Fig. 1). The first is lateral support of mountains from tectonic force, which either prevents mountains from falling apart under their own weight or pushes them farther up against gravity. The

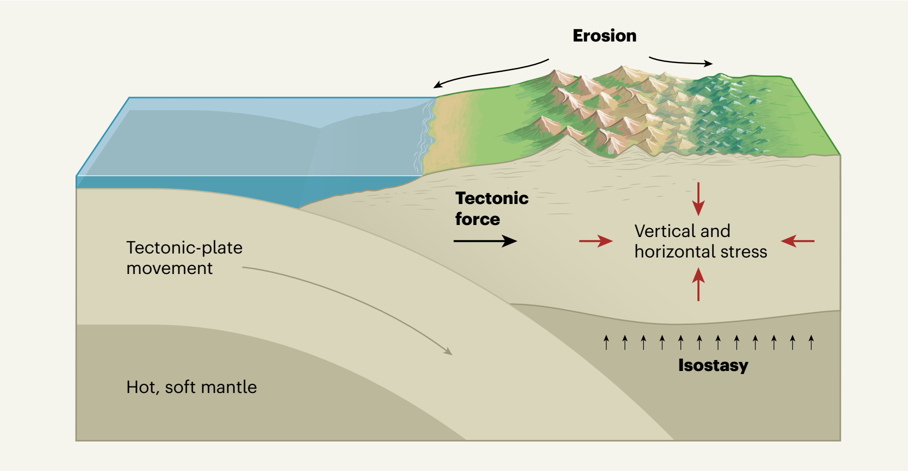

Figure 1 | Processes that control mountain height near convergent tectonic-plate boundaries. Three main processes control mountain height: lateral support of mountains from tectonic forces, which stops mountains from collapsing under their own weight or pushes them up against gravity; climate-controlled erosion; and isostasy, which keeps mountains afloat on the hot and soft mantle material. For mountains near subduction zones (regions where one tectonic plate dives beneath another to form a fault), the main tectonic force comes from the fault. By assuming that the horizontal and vertical stresses beneath such mountain ranges are equal, Dielforder *et al.*[3] estimate the mountain height that can be supported by the tectonic force at several locations. The estimated heights are similar to observed heights, thus suggesting that the heights are controlled by tectonic force, rather than by erosion. It remains to be seen whether the same is true at the many mountain ranges that are not close to subduction zones.

second is climate-controlled erosion, which limits mountain height by removing material from high elevations. And the third is a process known as isostasy, which keeps mountains afloat above the hot and soft mantle material in a similar way to icebergs floating in water. For the purposes of this discussion, we can ignore local-scale processes such as volcano growth due to magma activity.

Scientists all agree that the three main processes work together to maintain mountain heights in a dynamic fashion. Complications arise because the different processes might not keep pace with one another[4]. The scientific debate focuses on whether erosion can outpace tectonic force, or vice versa. The isostatic response to the other two processes is thought to be sufficiently prompt to keep pace, and therefore is usually not questioned in this debate.

The most representative of the models in which erosion controls mountain height is known as the glacial buzz saw. On the basis of observations of topography and glacier distribution, this model postulates that glacial erosion, in concert with isostatic uplift, keeps mountain heights at about the elevation of the climate-controlled snowline, regardless of the tectonic force at work[2].

Dielforder and colleagues now propose a different model that puts tectonic force in the driving seat. The primary tectonic force near convergent plate boundaries is provided by the major geological fault at the boundaries (Fig. 1). The authors estimate this force for various plate boundaries, using estimates of the strength of the associated faults and various thermal and mechanical parameters appropriate for each region considered[5]. The quantification of all of these parameters requires several assumptions to be made, thereby introducing some uncertainty into the estimates.

However, Dielforder and co-workers' most important assumption is used to forge a link between tectonic force and mountain height. The authors assume that stress in the crust directly beneath the mountains is in a neutral state – that is, horizontal compression due to the tectonic force and vertical compression due to the weight of the rock column are the same[6]. Because the weight of the rock column is proportional to its height, the tectonic force estimated for each plate boundary can thus be used to predict the mountain height that it can support. The authors find that the heights predicted by their model agree well with observed elevations. They therefore conclude that today's mountain heights are maintained by the tectonic force, regardless of climate conditions and erosion rates.

If tectonic force is the dominant control, how do we explain the previously reported correlation between mountain heights and climatic conditions[2,7]? The answer might lie in the regions examined by Dielforder and co-workers: most are subduction zones (areas in which one tectonic plate is sliding beneath another; Fig. 1), which, with the exception of the Andes, do not host very high mountains. Perhaps the previous results can be reconciled with the current study if a broader range of tectonic environments is examined.

Alternatively, if erosion is the dominant control, the tectonic force is still needed to balance the weight of the rock column. Areas that exhibit large topographic relief, such as that from a submarine trench to a mountain top (Fig. 1), generally need both isostasy and tectonic force to balance the weight. If a mountain range is kept low by climate-controlled erosion, does this implicitly indicate that the tectonic force is small? A related question is whether a given mountain height can be associated with only one possible value of the tectonic force. The answers require an understanding not only of the force, but also of the strength of the rocks.

Dielforder *et al.* provide a crucial argument in the mountain-height debate, but their perspective comes with its own dilemma. Tectonic force raises mountains by crushing and piling up crustal rocks. To keep up with erosion, it has to keep the crust on the verge of compressive failure. In accordance with commonly accepted ideas about the strength of the brittle upper crust, compressive failure requires the horizontal stress to be much higher than the vertical stress[8–10] – whereas Dielforder and colleagues assume that horizontal and vertical stress are of the same magnitude (a neutral state) beneath the mountains.

To solve this conundrum, the authors speculate that the crust in mountainous areas has almost no strength because it contains very weak faults, so that neutral stress is not far from failure. But if the crust is so weak, why don't the mountains collapse, and why don't these areas become plate boundaries? There is evidence that crustal stress is indeed almost neutral near some subduction zones[10], but it is not clear whether it is commonly neutral beneath high mountains. The mountain-height debate thus leads to a crustal-strength puzzle. Dielforder and colleagues' work suggests that much observational and theoretical research is needed to understand crustal stress and strength if we hope to resolve the issue of mountain height.

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