caused by a lack of cleavage by caspase-8.

Little is known about pathways downstream of the necrosome. Either reactive oxygen species or activation of autophagy through deregulated metabolism might be essential for the completion of programmed necrosis[14]. It has become clear, however, that the various death pathways are more closely intertwined than was previously thought. The crosstalk between the components regulating autophagy[15], apoptosis and necrosis[1–3] amply demonstrate that. ■

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EARTH SCIENCE

Continental jelly

An approach integrating different data sets has been used to map out seismic-velocity ratios in the crust of western North America. High inferred quartz content correlates with tectonic deformation zones. SEE LETTER P.353

ROLAND BÜRGMANN & PASCAL AUDET

Ever since the recognition of plate tectonics on Earth, with its jigsaw puzzle of shifting plates, geoscientists have wondered why otherwise strong and rigid continents repeatedly break up and collide along the same zones of apparent weakness. On page 353 of this issue, Lowry and Pérez-Gussinyé[1] propose that the inherent weakness of these persistent deformation zones may be caused by the low strength of quartz, and its relative abundance in such zones in the continental crust — Earth's outermost layer, which is generally 30–50 kilometres thick in continental regions.

The authors' data were drawn from the EarthScope Transportable Array of seismic stations in western North America, with additional constraints coming from gravity and heat-flow measurements. They used a new approach to develop a map of the ratio between pressure-wave (v_P) and shear-wave (v_S) propagation velocities in the crust from distant earthquakes (see Fig. 3 on page 355). On the basis of experimental data[2], Lowry and Pérez-Gussinyé argue that low values of this ratio (v_P/v_S of about 1.8 or lower) are uniquely associated with high concentrations of quartz in the crust, a mineral that flows much more readily than other crustal constituents at the high temperatures found at depth[3].

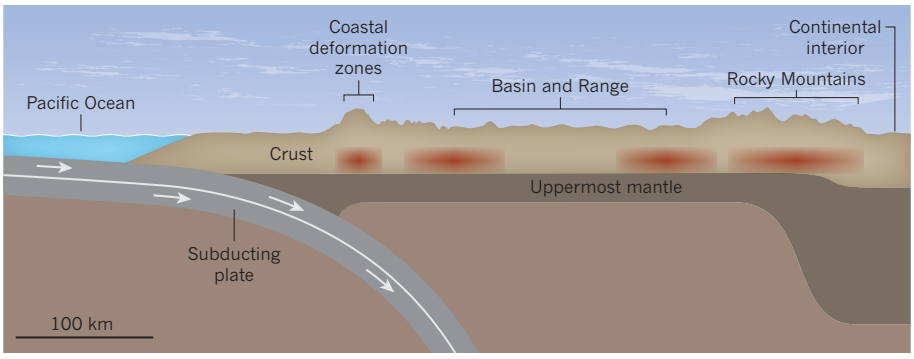

Figure 1 | Cross-section through zones of active deformation in western North America and the stable continental interior. At the left (west) is the subduction zone; at right, the stable continental interior. Lowry and Pérez-Gussinyé[1] find that regions of high inferred quartz content in the lower crust (red) correlate well with zones of recent tectonism exemplified by the coastal deformation zones, parts of the Basin and Range province and the Rocky Mountains. The thickness of the North American plate (crust and rigid uppermost mantle) decreases from more than 200 km in the interior to about 50 km in the west as a result of thermal thinning and hydration caused by past and present subduction.

The study region is the western Cordillera, reaching from the San Andreas fault system in California to the Rocky Mountains in Wyoming and Colorado. The apparent association of low v_P/v_S with zones of recently active plate-boundary deformation in this region suggests that high abundance of quartz-rich rocks in the lower crust, often described as a weak zone of jelly in the continental sandwich of crust and mantle[4], is a key ingredient for initiating deformation (Fig. 1). Once a deformation zone has been initiated, further weakening by rising temperatures and addition of fluids may sustain a permanently weak zone over many plate-tectonic cycles. Such inherited weakness may isolate continental interiors from deformation and force the repeated reactivation of plate-boundary faults during alternating cycles of plate divergence and convergence[5].

The method developed by Lowry and Pérez-Gussinyé relies on an automated data-analysis product[6], which calculates bulk crustal properties (v_P/v_S and crustal thickness, H) at several hundreds of seismic stations using converted pressure-to-shear-wave arrivals resolved on the radial component of motion. Those parameters are notoriously difficult to estimate accurately because of a well-known trade-off between H and v_P/v_S. To improve the resolution of the estimates, the authors use two additional constraints from statistical inference: optimal spatial interpolation and gravity modelling. The model uses gravity anomalies to obtain an optimal density structure that fits variations in v_P/v_S, H and additional contributions from heat-flow data. The technique thus cleverly combines disconnected data sets with statistical modelling to significantly improve the accuracy of the solution.

Nevertheless, the method is limited by the initial automated solution, which is obtained assuming a single-layer, isotropic crust with a flat crust–mantle boundary. Any deviation from this simple model, produced by non-horizontal structure, anisotropy or multiple layering, may produce complicated patterns of shear-wave arrivals on both radial and transverse components of motion; when inverted for the single-layer crust, interference patterns result that can bias the solution. One possible improvement to the method would be to use transverse-component shear-wave arrivals both to evaluate the validity of the single-layer crustal model and to help refine it.

There is some debate on where the strength of tectonic plates resides. In the traditional jelly-sandwich model of continental plate strength, a weak lower crust underlies a strong and brittle upper crust and overlies a strong uppermost mantle layer[4]. An alternative view is that the uppermost mantle contributes little to continental strength in many regions, leaving the brittle crust alone to support tectonic stresses[7].

Studies that model geodetically measured

deformation due to viscous flow of rocks induced by large earthquakes in western North America indicate that, at these short timescales, the lower crust is quite strong, whereas the upper mantle below about 50 km is much weaker[3,8]. The effective flow strengths of the lower crust found in the geodetic studies seem too high for the quartz-rich make-up suggested by Lowry and Pérez-Gussinyé. On the other hand, low, long-term static strength, inferred from estimates of effective elastic plate thickness of only 10 km or less (see Fig. 4 on p. 356), is consistent with a weak lower crust in the region. Thus, lower-crustal viscosities at very long (millions of years) timescales may effectively control the stability of continental crust and upper mantle[8].

Is a quartz-rich layer in the crust, only tens of kilometres thick, able to initiate break-up of a continental plate originally dominated by a strong mantle layer up to 200 km thick[9]? Lowry and Pérez-Gussinyé argue that, following initial deformation enabled by the quartz-rich crust, the strong mantle layer can be further softened by high temperatures and/or fluids derived from subducting oceanic plates[10], leading to the eventual loss or sogginess of the bottom slice of the jelly sandwich. Importantly, even where the uppermost mantle remains stable, as indicated by high estimates of elastic-plate thickness, a quartz-weakened lower crust can promote tectonic deformation. This may have been the case during the most recent tectonic period of the northern Rocky Mountains (Fig. 1), the Laramide orogeny[1].

The validity of the model can be tested when similar techniques are applied to different tectonic provinces that have experienced successive cycles of supercontinent formation and mountain-building. In particular, as Lowry and Pérez-Gussinyé suggest, the extension of the Transportable Array across older orogens in eastern North America during the next two years will provide a unique opportunity to test the role of quartz in mountain building. ■

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REPRODUCTIVE BIOLOGY

Progesterone's gateway into sperm

The hormone progesterone rapidly activates intracellular signalling in human sperm, regulating key aspects of their physiology. An ion channel unique to the sperm tail seems to relay progesterone's signal. SEE LETTERS P.382 & P.387

STEVE PUBLICOVER & CHRISTOPHER BARRATT

The ovarian hormone progesterone classically binds to a nuclear receptor, initiating gene transcription. But how does it stimulate the transcriptionally inactive human spermatozoon in preparation for fertilization? This question has long both fascinated and frustrated reproductive biologists. In this issue, Strünker and colleagues[1] and Lishko *et al.*[2] provide an unexpected answer: progesterone activates a sperm-specific calcium ion (Ca^{2+}) channel called CatSper.

For a sperm to reach the egg, it must penetrate the cumulus oophorus, a thick layer around the egg composed of granulosa cells embedded in a gelatinous matrix. These cells actively synthesize progesterone, such that its concentration within the cumulus is in the micromolar range. It was first reported more than 20 years ago[3] that progesterone, even at concentrations well below those present in the cumulus, induces immediate influx into human sperm of Ca^{2+} — a factor central to regulation of sperm function[4,5]. Progesterone is therefore believed to have a crucial role during the events leading to fertilization[6].

Sperm cells respond to progesterone within less than a second, which is characteristic of classical signalling pathways that involve cell-surface receptors[3,6]. Such non-nuclear actions of steroid hormones are quite common. In fact, progesterone and its related hormones are considered to have two distinct modes of action: through intracellular nuclear receptors, which regulate transcription; and through non-genomic receptors, probably at the plasma membrane, which regulate ion channels, G-protein-coupled receptors and signalling pathways mediated by kinase enzymes[7]. However, the mechanism of progesterone-induced Ca^{2+} influx in sperm has resisted all attempts at characterization, with even the type of 'receptor', let alone the nature of the Ca^{2+}-influx pathway, remaining a mystery. This has been particularly frustrating because the phenomenon is probably of considerable clinical significance: in human sperm, failure of progesterone-activated Ca^{2+} influx is correlated with reduced fertility[6].

The solution to this mystery follows directly from two crucial advances in the field. First, in 2001 two groups[8,9] reported the discovery of the Ca^{2+}-permeable cation channel (CatSper), which is expressed only in the plasma membrane of a domain in the sperm tail called the principal piece. Sperm from genetically manipulated mice that cannot express CatSper have impaired motility and, crucially, cannot display hyperactivation — an extravagant, highly asymmetric form of flagellar beating that is regulated by Ca^{2+} and is essential for fertilization. CatSper-deficient male mice are infertile.

The second, more recent, advance was the development of a method for applying to sperm the technique of whole-cell patch clamping, which records ionic currents across the entire plasma membrane of a cell. Using this technique, researchers showed that increased alkalinity of the sperm cytoplasm strongly activates CatSper channels, promoting Ca^{2+} flux into the cell. Strünker *et al.* (page 382) and Lishko and colleagues (page 387) now use this powerful technique to elucidate the mechanism by which progesterone induces rapid Ca^{2+} influx into human sperm.

Progesterone-induced membrane currents have identical characteristics to those carried by CatSper. For instance, the biophysical aspects of the currents are indistinguishable, with both progesterone and increased intracellular pH stimulating CatSper by shifting its voltage sensitivity so that it opens at lower voltages (Fig. 1). What's more, pharmacological manipulation has the same effects both on CatSper currents activated by increasing intracellular pH and on those stimulated by progesterone; applied together, progesterone and increased alkalinity act synergistically[1,2].

The effect of progesterone on CatSper is not simply a nonspecific effect of steroid hormones: another steroid hormone, oestradiol, has no effect on this channel[2]. However, several prostaglandins — non-protein mediators that increase intracellular Ca^{2+} concentration in human sperm — have strikingly similar effects to progesterone. Moreover, Strünker and colleagues' measurements of intracellular Ca^{2+} concentration in progesterone-stimulated sperm showed that compounds that block CatSper currents also reduce the progesterone-induced rise in Ca^{2+} concentration, and that