by a prostaglandin-independent mechanism. Gordon et al. demonstrate astrocyte-mediated dilation of arterioles in solutions containing 20% oxygen, which produces approximately physiological levels of oxygen in brain slices. They also find that astrocyte-mediated constriction occurs in solutions containing oxygen levels well above the physiological (95%). Why has evolution produced the latter pathway, in which neural activity decreases blood flow? And will physiological tissue concentrations of oxygen ever be high enough to activate this pathway? It turns out that 20-HETE-mediated arteriolar constriction is inhibited by nitric oxide (NO), a molecule that is released by neurons in response to glutamate secreted by neighbouring neurons (and which can also directly dilate arterioles). The 20-HETE-mediated pathway may therefore be better viewed as a mechanism producing a basal constriction of arterioles that can then be modulated by NO to provide another pathway for activity-dependent dilation.

Future work is likely to focus on how changes in the levels of lactate, adenosine, oxygen and NO interact to coordinate blood flow and hence the brain's energy supply. Some clues can be found in previous data. For example, NO released by neurons inhibits the conversion of arachidonic acid to epoxygenase derivatives that evoke dilation. As NO production in neurons requires oxygen, at low oxygen levels this mechanism will be inhibited, promoting dilation. Moreover, oxygen is needed for the synthesis of both constricting (20-HETE) and dilating (prostaglandin E$_2$ and epoxygenase) derivatives of arachidonic acid. At low oxygen levels, however, the production of 20-HETE is inhibited more strongly than that of prostaglandin E$_2$ and epoxygenase derivatives, increasing dilation. Finally, in blood capillaries, where contractile cells called pericytes may regulate blood flow, lactate causes constriction at high oxygen levels, but dilation at low levels. There is, therefore, an array of switching mechanisms that promote brain energy supply when oxygen levels fall.

In a wider context, Gordon and colleagues’ observations raise questions for both cognitive neuroscientists and neurologists. Could the initial dip in local oxygen concentration that accompanies neural activity affect astrocyte signalling rapidly enough to contribute to the increase in blood flow that generates the signals seen in functional imaging of the brain? And could our new understanding of astrocyte signalling lead to better therapies for correcting disorders of blood flow in the brain, such as those that occur after stroke and in vascular dementia?

Gordon et al. have opened a fresh chapter in our investigation of how blood flow is regulated in the brain. But their work has a broader implication: physiological studies using solutions bubbled with 95% oxygen may be altering the operation of signalling pathways in the brain, producing misleading results.

Catherine N. Hall and David Attwell are in the Department of Neuroscience, Physiology and Pharmacology, University College London, London WC1E 6BT, UK.

e-mail: d.attwell@ucl.ac.uk

a TEM, Sun et al. observed a highly perfect atomic structure with occasional grain boundaries and planar stacking faults. But dislocations were not visible. On the basis of molecular-dynamics simulations, Sun et al. argue that deformation originates from individual, transient dislocations that are freshly nucleated and vanish so fast that they cannot be seen with a TEM. Although diffusive atomic processes could be active at 300 °C in gold, the authors argue that diffusion does not contribute to plastic strain, and that the observed strength and deformation can be accounted for solely by the nucleation and motion of short-lived dislocations.

One of three competing mechanisms, all dependent on temperature and mechanical strain rate, induces plastic deformation: displacive, diffusional or mixed plasticity. Displacive plasticity is produced by the collective shearing of atoms, that is, the glide of dislocations. Diffusional plasticity is governed by many, almost random, individual atom or vacancy hops. In conventional coarse-grained metals, typically below about 0.25 T_M/3, where T_M is the absolute temperature at melting, deformation is dominated by displacive mechanisms, whereas above about 2T_M/3 diffusional mechanisms control the process. A mixture of these two mechanisms occurs at in-between temperatures; in such cases the inelastic strain is still mainly produced by dislocation glide but its rate is controlled by diffusion (Fig. 1c).

Lack of understanding of the deformation mechanisms that can operate in ultra-strong materials severely limits our ability to create nanometre-scale systems with the desired mechanical properties. Information about deformation mechanisms is often gathered from molecular-dynamics simulations, but these are limited to unrealistically high strain rates. Recently, progress has been made through the use of computational methods that elucidate mechanisms of displacive plasticity at low temperatures through direct calculations of the activation volume, which characterizes the sensitivity of plastic-yield stress (the stress at which the material deforms permanently) to strain rate. Such computational studies reveal that low-temperature deformation of ultra-strong systems, such as the nanocrystals studied by Sun et al., become highly sensitive to strain rate and temperature. The underlying mechanism involves the nucleation, absorption and desorption of dislocations from interfaces and free surfaces, with a resultant reduction in activation volume, typically 2–20 times the volume of a single atom (Ω_0). This activation volume is much smaller than those observed for traditional displacive-plasticity mechanisms (about 10^7 Ω_0) that operate in coarse-grained polycrystals. It is, however, still larger than those of typical vacancy processes, for which the activation volume is less than about Ω_0.

But at higher temperatures, such as 300 °C in gold, the way deformation changes with strain rate and the scale of nanostructures is unknown. In particular, the temperature and stress boundaries that separate the displacive processes from the diffusional and mixed processes will shift from those of the corresponding coarse-grained materials. Further experiments and modelling at higher temperatures will inevitably be needed to understand deformation in nanostructured materials. Meanwhile, Sun et al. have developed an innovative in situ experimental method that could provide insight into the process.

Subra Suresh is in the School of Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA.
Ju Li is in the Department of Materials Science and Engineering, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA.