MATERIALS SCIENCE: Fluctuations in Plasticity at the Microscale

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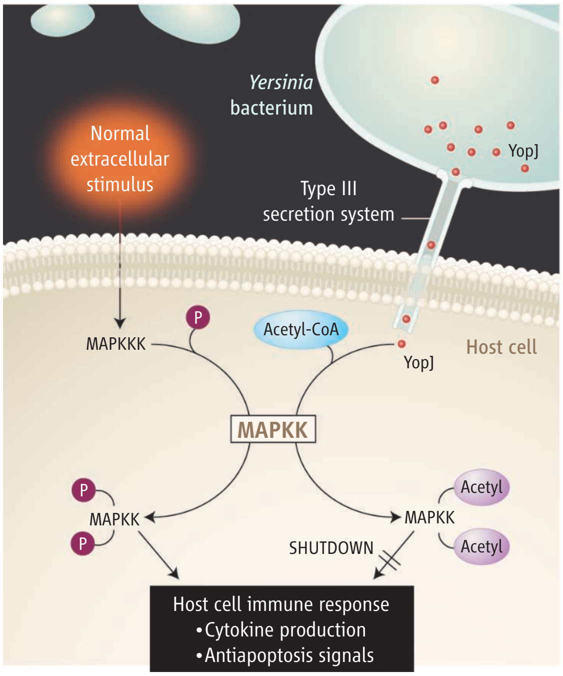

Virulence factor interference. YopJ that is deployed into a host cell blocks a signaling pathway by modifying the enzyme MAPK kinase (MAPKK) with acetyl moieties. This prevents activation of MAPKK by phosphorylation (P) via MAPKKK, and shuts down the immune response.

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lar to a triad found in ClanCE cysteine proteases, which include AVP and the ubiquitin-like protease (Ulp-1) (*8*). Orth *et al*. (*7*) showed that YopJ can hydrolyze SUMO-1, a ubiquitin-like protein, from SUMO-1–conjugated proteins. Using a similar rationale, Zhou *et al*. (*9*) demonstrated that YopJ can function as a deubiquitinase. Neither of these observations, however, explains the ability of YopJ to specifically inhibit the MAPK pathways at the level of the MKKs. In light of the new data, it seems likely that the above observations may represent global cellular effects that can be obtained when a protein, usually expressed at low levels, is overexpressed in cells.

Mukherjee *et al.* show that YopJ is an acetyltransferase that blocks activation of the MAPK and NFκB pathways by acetylating serine and threonine residues on MKK6 and IKKβ. The authors used an in vitro system to recapitulate the ability of YopJ to inhibit the phosphorylation of MKK6. Subsequent analysis of MKK6 demonstrated that YopJ acetylates MKK6 on the serine or threonine residues critical for kinase activation, thus directly blocking its activation by phosphorylation. In addition, IKKβ is also acetylated on the two residues that are normally phosphorylated in its signaling cascade. Therefore, in each case, acetylation effectively blocks the ability of upstream kinases to phosphorylate and activate these proteins, thereby preventing the activation of downstream effectors. Although the details of the enzymatic posttranslational modification are yet to be worked out, most likely the cysteine residue of YopJ catalyzes the transfer of the acetyl group from acetyl-CoA to YopJ, forming an acyl enzyme intermediate. The acetylated form of YopJ then transfers the acetyl group to the reactive serine or threonine residues of MKK6 and IKKβ.

This activity for YopJ elegantly explains its ability to block phosphorylation of MKK6 and IKKβ and raises the interesting question of whether other MKKs present in parallel MAPK pathways also undergo similar modifications. This in turn raises other questions: Do other members of the YopJ family function as acetyltransferases? Do eukaryotic cells have acetyltransferases whose normal function is to regulate fluxes through the MAPK pathways, and do novel acetyltransferases exist to block sites of phosphorylation in other pathways? Hart and colleagues have suggested that glycosylation plays a similar role in blocking phosphorylation (*10*). Taken together, the direct competition of one posttranslational modification for another may be a more common cellular strategy for regulation of flux through signal transduction pathways than previously recognized.

Knowing that YopJ functions as an acetyltransferase is not the end of the story. It is really the beginning of what is likely to be the exciting search for other acetyltransferases in bacterial pathogens and viruses as well as in eukaryotic cells.

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MATERIALS SCIENCE

Fluctuations in Plasticity at the Microscale

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During deformation, microscale materials may flow or change shape abruptly as atomic-scale defects migrate and assemble. The abrupt episodes of deformation appear to have a power-law distribution, a finding that may help in the design of miniature devices.

A fundamental challenge in materials science today is the investigation of size effects that influence the mechanical properties of micrometer- to nanometer-scale devices. These small scales are ubiquitous in modern technological applications and pose new theoretical questions as a result of the crucial role played by fluctuations. These fluctuations are observed as step changes or discontinuities in the mechanical response caused by the inhomogeneous dynamics of defects at the microscale. Fluctuations of this kind become more important as the size of any physical system decreases, hence they can lead to substantial deviations from the system's average behavior. On page 1188 of this issue, Dimiduk and co-workers (*1*) report experimental results on metal microcrystals that provide direct evidence of scale-invariant intermittent plastic flow—that is, permanent deformation with strain bursts that have a power-law distribution. These high-resolution experiments call for a novel theoretical framework that could help unravel microscopic deformation behavior in crystalline materials.

Plastic deformation is often described as a smooth process occurring in an elastic continuum. Yet microscopically it is due to the nucleation and motion of discrete crystal defects, known as dislocations. Dislocations self-assemble into intricate structures that determine the mechanical properties of a crystalline material. When external forces are applied, these dislocation structures dis-

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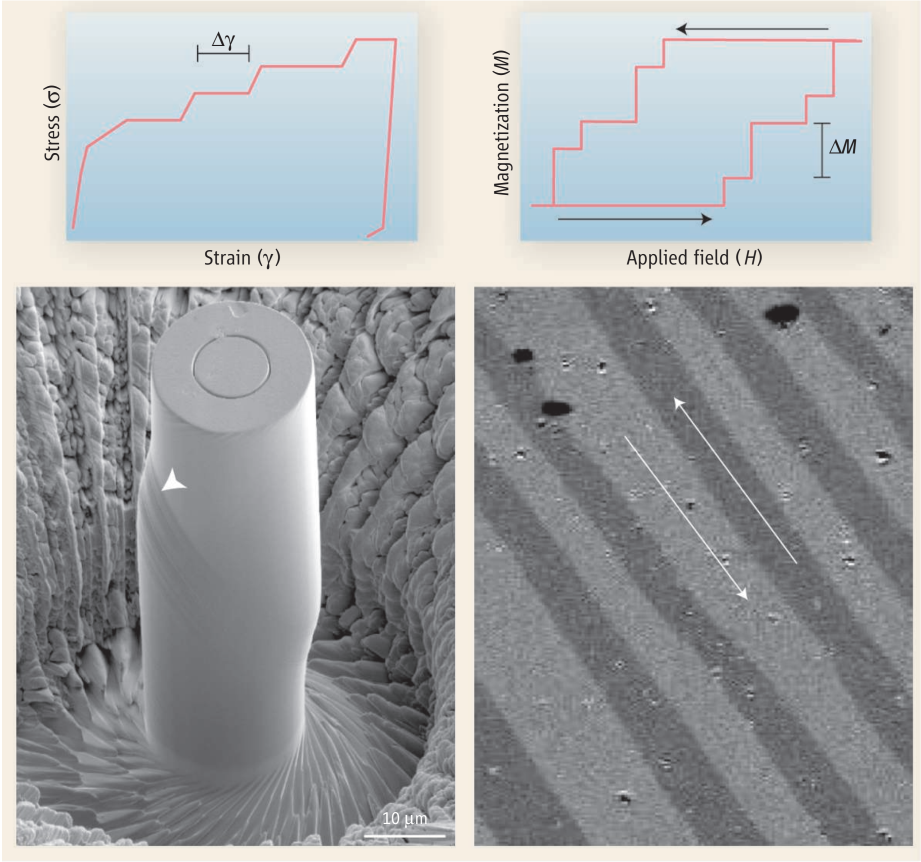

Plastic deformation of crystalline materials resembles ferromagnetic hysteresis. **(Top)** The bursts in a typical stress-strain curve from a micrometer-size sample **(left)** are analogous to the magnetization jumps in a hysteresis cycle of a ferromagnetic thin film **(right)**. **(Bottom left)** A cylindrical nickel sample after compression shows sloping slip planes (arrowhead) formed by motion of dislocations. **(Bottom right)** A magneto-optical image of a ferromagnetic alloy, where magnetization is due to the motion of domain walls (arrows).

entangle and become mobile, giving rise to plastic strain. Conventional analysis based on continuum models presumes that the microscopic details of this flow average out above a given size scale, so that fluctuations can safely be ignored.

The powerful experimental methodology developed by Dimiduk *et al.* and Uchic *et al.* (*2*) to manipulate small crystals challenges this viewpoint. Uniaxial compression testing of nickel crystals gives rise to staircase-like stress-strain curves (see the figure, top left) and, at the same time, leads to the formation of slip bands on the sample's surface (figure, bottom left), indicating dislocation-mediated deformation. Moreover, the yield stress, which separates elastic and plastic behavior, increases, as does its fluctuation, as the sample size is decreased (*2*). These experimental results exhibit some common features characteristic of other systems driven out of equilibrium. Bursts of activity (avalanches) and power law–distributed crackling noise are observed in a wide variety of physical systems, but, in particular, they are expected in the close vicinity of a critical point (*3*). Are all these mechanical observations thus interpretable within the realm of statistical mechanics, or more precisely, within the scenario of nonequilibrium phase transitions?

Dislocation dynamics models suggest that the onset of plasticity corresponds to a nonequilibrium phase transition, controlled by the external stress, that separates a jammed phase, in which dislocations are immobile, from a flowing phase (*4*). When the external stress σ is raised toward the yield stress σ_Y, the material responds by larger and larger dislocation avalanches, whose characteristic size diverges at σ_Y. Right at this point, the plastic strain γ would grow indefinitely. We may wonder why macroscopic deformation looks smooth if the internal strain avalanches are scale-free. An important fact is that when most materials deform, the dislocation density increases, leading to strain hardening: The stress required to sustain plastic flow increases with deformation, as if an additional back-stress $\sigma_b = -\Theta\gamma$ were building up inside the crystal (where Θ is a phenomenological coefficient). The back-stress opposes the propagation of large plastic avalanches, inducing a finite characteristic size. For this reason, we do not normally see steps in the stress-strain curves, although dislocation avalanches can still be revealed when probing small scales in acoustic emission experiments (*5*).

The scale-invariant strain bursts observed in crystal plasticity have a counterpart in ferromagnetic materials. In thin films, for instance, irregular steps in the magnetization curve can be seen by magneto-optical methods (*6*) (see the figure, top right). These steps reflect the erratic dynamics of domain walls, separating regions of opposite magnetization M (figure, bottom right). Domain walls are pinned by the impurities present in the material and start to move, magnetizing the sample, when the applied magnetic field H overcomes the coercive field H_c, in a way analogous to dislocations at the yield stress. In addition, large domain wall avalanches are hindered by dipolar interactions that induce a demagnetizing field opposed to the magnetization: $H_d = -\kappa M$ (where κ is the demagnetization factor) (*7*). Thus, hysteresis loops appear smooth in thick samples but look more irregular in thin films where κ vanishes. The close analogy between plasticity and magnetism, which are two apparently very different problems, provides a vivid illustration of the principles of complexity: Collective phenomena often obey simple rules, regardless of the distinctive details.

The experimental results presented by Dimiduk *et al.* open the way to understanding and possibly controlling fluctuations in plastic deformation. This is a topic of great technological importance in view of the current trend toward device miniaturization. Furthermore, this understanding could pave the way for a microscopic theory of the yielding transition of interacting dislocation assemblies. Although this represents a formidable task, important steps in this direction have been taken recently by Zaiser and Moretti (*8*). The theoretical conditions they study are not far from those in the experiments by Dimiduk and co-workers, and indeed the value of the experimentally measured power-law exponent (*1*) is explained by the theory (*8*). These results confirm that plasticity is an excellent playground for statistical mechanics methods and ideas.

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