silencers. Moreover, the authors observed that the SPOC domain interacts with parts of the machinery used for transcription and splicing (the process by which newly made RNA transcripts are turned into messenger RNA), including RNA polymerase II, the enzyme that catalyses transcription. Dossin and colleagues identified interactions with components of the N^6-methyladenosine (m^6A) methyltransferase complex, several of which have been linked to XCI[6,11,15]. Accordingly, SPEN and its array of associated proteins might function like a molecular multi-tool to silence genes in various genomic contexts. Although much of SPEN's silencing function might derive from its interactions with known epigenetic silencers, its association with transcription and RNA-processing machineries leaves open the possibility that SPEN can also silence genes through another, as-yet-undefined mechanism.

Perhaps most strikingly, Dossin *et al.* adapted a technique called CUT&RUN to map the location of SPEN on an X chromosome that was being inactivated. This revealed that, shortly after *Xist* starts to be expressed, SPEN associates with active gene promoters and enhancers (DNA regions that initiate and increase the likelihood of transcription, respectively), but then disengages from these sites after it has silenced transcription. These discoveries imply that SPEN is part of a system that recruits silencing machinery specifically to transcriptionally active regulatory elements at the onset of XCI (Fig. 1). Whether this mechanism also requires chromatin modifications, RNA polymerase II, actively transcribed RNA or other factors should be addressed in the future. Another issue that should be investigated is why *Xist* isn't silenced by SPEN, given that a large amount of SPEN accumulates over the *Xist* gene.

SPEN binds to a region of *Xist* RNA called Repeat A, which is required to initiate gene silencing[5,8,16]. Because deleting the *Spen* gene largely mirrors the effects of deleting Repeat A (ref. 11), SPEN seems to be responsible for most of Repeat A's silencing ability. However, Repeat A also binds to other proteins, including those that normally promote splicing, as well as to RBM15 and RBM15B, SPEN's SPOC-domain-containing cousins[5,15,17]. Therefore, it is now crucial to determine how these proteins might compete or cooperate with SPEN to initiate gene silencing. Moreover, deletion of Repeat A drastically reduces levels of the *Xist* RNA itself[18], and, in certain contexts, deletion of SPEN similarly reduces levels of *Xist*[11]. How Repeat A is required for the production of *Xist*, and how its role in *Xist* production relates to its ability to initiate silencing, are key questions for the future.

For decades, *Xist* has served as a leading example of RNA's role in regulating gene expression. Most notably, *Xist* was one of the first mammalian RNAs shown to be involved in Polycomb-mediated silencing[3,4]. It therefore seems appropriate that, by studying this RNA, Dossin *et al.* might have uncovered a new and fundamental aspect of gene regulation — the transient recruitment of SPEN to regulatory elements by RNAs, or even by proteins, which could be a general mechanism for silencing transcription throughout the mammalian genome.

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Materials science

Why surface roughness is similar at different scales

Astrid S. de Wijn

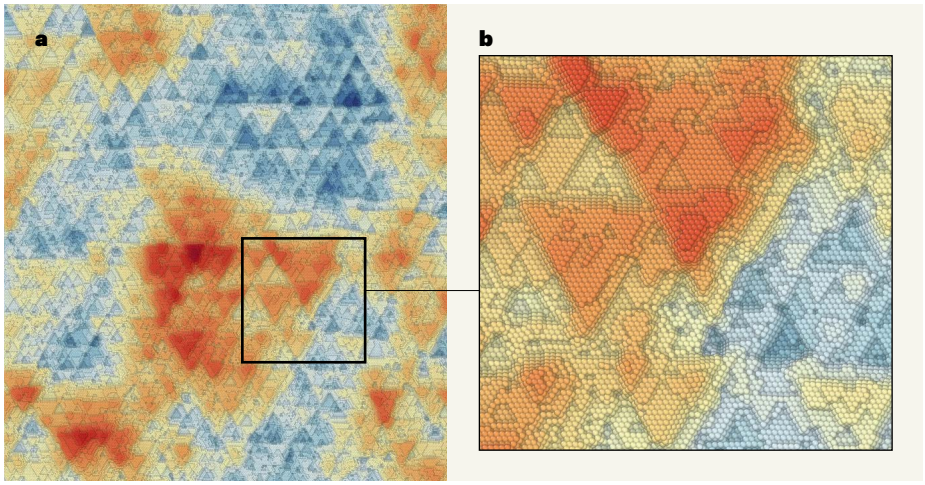
Most surfaces are rough at many length scales. Simulations show that this characteristic originates at the atomic level in metal-based materials when smooth blocks of these materials are compressed.

Almost all solid surfaces are rough. This roughness occurs at length scales that encompass 13 orders of magnitude — from the kilometre-scale peaks of mountains, down to atomic-scale bumps. Roughness seems to emerge regardless of what is done to a surface. Yet there is little understanding of how this roughness comes about, and especially why it is often self-affine, meaning that a surface looks similar on different length scales. Writing in *Science Advances*, Hinkle *et al.*[1] show that self-affine roughness has its origin at the atomic level.

As anyone who has ever slipped on a wet floor will have noticed, the roughness of surfaces can have a crucial role in practical situations. Smooth surfaces are slippery when wet, but are also easier to lubricate inside moving machinery than are rough surfaces. By contrast, we sand surfaces before painting them to make them rougher, and thereby to increase the adhesion of the paint. The effects of roughness are less straightforward in other situations: for example, the roughness of the surfaces of skis and snowboards affects their friction on snow differently depending on the temperature and humidity[2]. Engineers have therefore developed many techniques to control surface roughness, such as grinding, polishing and so on. Hinkle and colleagues' results help us to understand better how roughness emerges, and thus might provide new ideas for how to control it.

The authors carried out computational simulations of three materials: a single, perfect gold crystal, an alloy and a metallic glass. These materials have very different amounts and types of disorder, which means that roughness might be expected to develop through different mechanisms or to have different characteristics for each of them. Because the deformation of a material is likely to contribute to the formation of roughness, the researchers simulated the compression of flat blocks of these materials beyond their elastic limit — that is, at forces that cause irreversible (plastic) deformation. Because the length scales of the effects the researchers were looking for span several orders of magnitude, the simulations had to be quite large, containing tens of millions of atoms. Such simulations are computationally extremely expensive.

Hinkle and colleagues investigated how fluctuations in the roughness produced in the simulations change when the size of the area being observed is increased. They observed that the roughness profiles of all three materials seem to obey a power law — that is, they do indeed display self-affine scaling, over nearly two orders of magnitude (from about 1 nanometre up to the size of their



REF. 1

Figure 1 | Roughness on a simulated gold surface. Hinkle *et al.*[1] carried out molecular-dynamics simulations of tens of millions of atoms in smooth blocks of three materials, including gold (shown here), and observed how surface roughness develops when the blocks are compressed. Colours represent atomic positions perpendicular to the surface, measured relative to the surface's mean height: red indicates high topography; blue, low. The highest features are 8.8 nanometres above the lowest point on the surface. The authors found that roughness emerges that is similar across nearly two orders of magnitude of length scales. Similar triangular features and variation of topography are visible in **a** (a region 80 nm across) and **b** (a region of **a** expanded to four times its original size). The same is also true at magnifications of 8 and 64 (not shown).

simulation 'box', which was approximately 70–100 nm; Fig. 1).

In addition to simulating millions of atoms, the authors simulated a continuum model of compressive deformation in which the material is not treated as being composed of individual atoms, but as a continuous medium. In these simulations, there is no sign of self-affine roughness. The authors therefore conclude that the development of self-affine roughness is related to atomic-scale fluctuations in plastic flow that are missing from the continuum model.

Hinkle and colleagues' results are convincing across the observed length scales, but the scaling behaviour of the roughness will need to be demonstrated across three orders of magnitude to confirm that it truly obeys a power law. This will require the atomic simulations to be extended to even larger scales. Modelling techniques (see ref. 3, for example) are available at mesoscale lengths (which range from a few nanometres to several hundred micrometres), and provide a link between atomistic and continuum simulations. These approaches take flow into account in more detail than does the continuum model used by Hinkle *et al.*, and would allow for increased atomistic detail and fluctuations in simulations. This could help to provide the extra order of magnitude needed to convincingly show the power-law statistics of the roughness.

It remains to be seen how universal the reported behaviour is. All of the materials investigated by Hinkle and co-workers are based on metals. After undergoing plastic deformation, they are all homogeneous (there is only one type of solid phase in the material) but disordered, and the dynamics and energy scales involved in atom displacement are all comparable. It would be interesting to see whether similar scaling behaviour emerges from the compression of other types of material that have different mechanisms of plasticity and deformation, such as polymers. If so, are the scaling exponents — the key scaling parameters in the power-law equation — the same for all materials? If roughness profiles can be extended to include one or more extra orders of magnitude, it would enable a reliable comparison of the scaling exponents. This, in turn, would help to determine whether these exponents vary with strain, deformation mechanisms, or even time.

Power-law behaviour is common in plastic deformation. For example, 'avalanches' of plastic deformation occur in metals[4], and in fibrous materials a power law describes the size distribution of avalanches when these materials deform plastically under tensile stress[5]. Given that Hinkle *et al.* simulate the formation of rough surfaces in response to plastic deformation, and also observe scale-free roughness in the bulk of the modelled materials, it seems likely that there is a link between the development of self-affine roughness and the power-law behaviour of plastic deformation events — as the authors also note. It would therefore now be interesting to study the emergence of roughness in a more dynamic way, by investigating the formation of roughness features during compression, and relating the changes in the surface profile to plastic events.

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Cancer

Loss of p53 protein strikes a nerve for tumour growth

Marco Napoli & Elsa R. Flores

Tumours often grow entangled among neurons, which makes the cancer difficult to treat. The finding that cancer cells hijack neighbouring neurons to promote tumour growth suggests new therapeutic targets. **See p.449**

Malignant tumours are a complex, yet organized, diverse ensemble of cells. Tumour cells are surrounded by other types of cell, which collectively form the tumour microenvironment. Components of this microenvironment include fibroblast cells, which can promote the growth and spread of tumours to distant sites, and immune cells. The latter have antitumour functions that are often suppressed by cancer cells; indeed, therapies that boost such immune cells are revolutionizing the treatment of certain cancers. By contrast, the interactions between cancer cells and neurons in the tumour microenvironment are less-well understood. On page 449, Amit *et al.*[1] reveal how tumours influence neurons to promote tumour growth, and show how this discovery might lead to new anticancer therapies.