of the twentieth. Both presidents seem to have engaged in politically reckless conduct; in Jefferson's case, fathering Eston six years after allegations appeared in the national press. And both offered evasive denials to the charges. In 1805 the Massachusetts legislature staged a mock impeachment trial of Jefferson, citing several grievances including the accusations about Sally Hemings. Jefferson acknowledged one charge (propositioning a married woman in his youth), but asserted that all the others were false. Otherwise he remained silent, leaving denials to political supporters and family. Nor did the scandal affect Jefferson's popularity. He won the 1804 election by a landslide, and his abiding position was that his private life was nobody else's business, and should have no bearing on his public reputation.

Foster and colleagues' findings renew questions about Jefferson's tortured position on slavery. If Jefferson's relationship with Hemings began in the late 1780s, it would mean that he began to back away from a leadership position in the anti-slavery movement just around the time that his affair with Sally Hemings started. Jefferson's stated reservations about ending slavery included a fear that emancipation would lead to racial mixing and amalgamation. His own interracial affair now personalizes this issue, while adding a dimension of hypocrisy.

Over the past 30 years, research into Jefferson has cast a shadow over his credibility as America's prophet of freedom and equality. Recent work has also emphasized his massive personal contradictions and his dexterity at playing hide-and-seek within himself. The new evidence only deepens the paradoxes.

Jefferson is, with Abraham Lincoln and George Washington, one of America's secular saints. His face looks out from the nickel, the two-dollar bill, the memorial near the Tidal Basin, and Mount Rushmore. His unique capacity to project inspirational words and ideas onto American public life has made him all things to all people. As an icon, Jefferson's legacy has been reinterpreted by every generation. Now, with impeccable timing, Jefferson reappears to remind us of a truth that should be self evident. Our heroes — and especially presidents — are not gods or saints, but flesh-and-blood humans, with all of the frailties and imperfections that this entails. □

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Quasicrystals

From tilings to coverings

Knut W. Urban

Quasicrystals occur in a great number of alloys, most of which consist of aluminium and transition metals. They were discovered[1] in 1984, being revealed by a rotational symmetry of X-ray or electron diffraction patterns (for instance, five-fold or ten-fold) which is impossible for true periodic crystals. Since then, physicists have wondered why atoms form in these complex patterns rather than in a regularly repeating periodic crystal. On page 55 of this issue[2] Paul Steinhardt and colleagues present an analysis of new electron microscope data that supports a simple answer to this question.

Although a quasicrystal is non-periodic, its structure still follows a subtle construction plan. Mathematically, this can be described with reference to a higher-dimensional analogue of a cubic lattice: the atom arrangement of an icosahedral quasicrystal (which is quasiperiodic in three dimensions) can be constructed starting from six-dimensional space; the decagonal quasicrystal (whose lattice is quasiperiodic in a plane but periodic along the third dimension) requires reference to five-dimensional space. But why should atoms care about higher-dimensional spaces? The mathematical recipe to describe the lattice does not give us any hint as to how the atoms manage to create it.

Ten years before their discovery in nature, quasiperiodic patterns with the same geometric properties as those calculated from five-dimensional hyperspace were described by Roger Penrose[3]. These are tilings of the plane, in which a set of suitable tiles is arranged without gaps or overlaps according to certain matching rules. An example (Fig. 1) is the set consisting of two rhombuses with edges of equal length, one with angles of 36° and 144° and the other with angles of 72° and 108°. Their edges are marked with single or double arrows, and the rules constrain adjacent tiles to have matching arrow types along their shared edge. Corresponding matching rules have been found for three-dimensionally quasiperiodic patterns based on two types of rhombohedron[4].

It would appear that Penrose's 'edge' rules can be used to mimic growth of quasicrystals by stepwise addition of tiles to a seed. However, because these rules are strictly local in nature, they are not enough to guarantee a defect-free quasiperiodic pattern[5]. A solution to this growth problem is instead to adopt 'vertex' rules[6], which can be interpreted in terms of short-range interactions between atoms in clusters centred on a given vertex. But this mathematical exercise is of little use to the physicist who wants to understand why and how quasicrystals form, as the tiles correspond neither to atoms nor to real atom clusters.

Figure 1 **Penrose's planar quasiperiodic tiling. It is formed by a set of two rhombuses with edges of equal length, one with angles of 36° and 144° and one with angles of 72° and 108°. Their edges are marked with single or double arrows, and the rules constrain adjacent tiles to have matching arrow types along their shared edge.**

In 1991, Sergei Burkov[7] realized that planar quasiperiodic tilings can be generated with only a single tile, a decagon, provided that the tiles can overlap. Five years later, Petra Gummelt[8] gave a mathematical proof that a quasiperiodic Penrose tiling can be generated using a single decagon combined with a novel overlapping rule. This rule is realized by decorating the interior of the decagons (Fig. 2) with a subset of shaded tiles, and two decagons may overlap only if shaded areas overlap. This is equivalent to Penrose's arrow matching rules[9]. In tilings overlapping has to be avoided as a point of principle. Here it becomes a basic construction element; so, using an established mathematical term[10], Gummelt called the pattern a 'coverage'.

Hyeong-Chai Jeong and Steinhardt[9] then proved that Penrose matching rules can be abandoned altogether and replaced by the condition that the density of a suitably chosen cluster (for instance in the form of Gummelt's decagon) is maximized. And this is where mathematics at last leads to physics. Jeong and Steinhardt concluded that quasicrystals represent a packing of a single type of atom cluster. This cluster can share atoms with its neighbours, and the resulting quasiperiodic pattern is just the one that maximizes cluster density. By postulating that this cluster corresponds to a minimum-energy atom configuration, the authors arrived at a physically plausible picture.

Striking evidence for the coverage model

now comes from electron microscopy on decagonal $Al_{72}Ni_{20}Co_8$. Steinhardt and colleagues[2] present micrographs that demonstrate the existence of Gummelt's decagonal coverage in nature. They used the high-angle annular dark-field technique[11]. In contrast to classical high-resolution transmission electron microscopy, where contrast interpretation requires a careful quantum-mechanical simulation of the dynamic imaging process (often with rather ambiguous results), the dark-field technique is based on high-angle scattering of a fine beam of electrons at atom cores in a scanning transmission electron microscope. In this case the imaging process is essentially kinematic in nature and allows a direct, intuitive image interpretation in terms of atomic structure. This makes the new results superior to those of previous studies in which atomic matching of classical high-resolution images to model lattices has been claimed.

Steinhardt and colleagues call the decorated decagon a 'quasi-unit cell' to emphasize similarities to ordinary crystal lattices. Whether this is a happy choice is questionable as clusters often also play a role in crystals; an example is the Frank–Kasper phases (where clusters occur which are quite similar to those found in quasicrystals). But these clusters never coincide with the crystal unit cells.

That clusters are important for quasicrystal formation was noticed quite early on[12,13]. In particular, the model of icosahedral Al–Pd–Mn, the quasicrystal of highest structural quality available today, is based on a 52-atom icosahedral cluster[14]. In this case it could even be shown that it owes its particular stability to a low electron energy[15]. In its present form, however, this model does not explicitly involve cluster overlap as a construction principle, but employs 'connecting units' which are interpenetrating pieces of the elementary cluster. Indeed, the new 'covering' model has still to be tested for three-dimensionally quasiperiodic quasicrystals. But the idea that the particular structure of quasicrystals is the consequence of maximizing the density of a low-energy atom cluster and (what appears to be particularly important) the experimental observation of the Gummelt coverage, make it worth while revising current models to incorporate this new view of quasicrystal formation. □

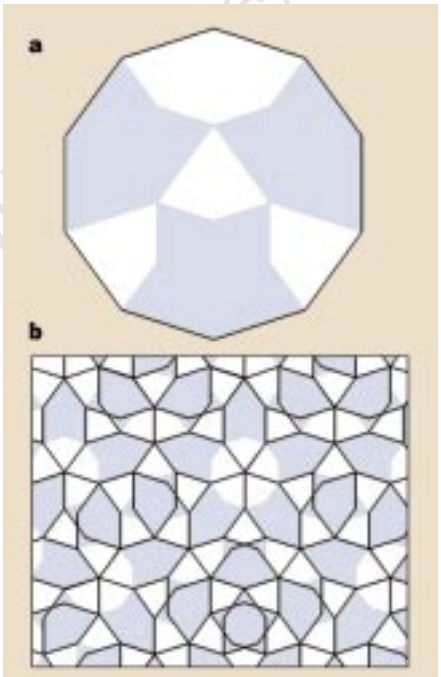

Figure 2 **Gummelt's planar quasiperiodic coverage.** a, **Gummelt's decorated decagon. The matching rule demands that two decagons may overlap only if shaded areas overlap.** b, **The resulting quasiperiodic decagonal coverage of the plane.**

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Inflammation

A new target for aspirin

Edward A. O'Neill

"Take two aspirin and call me in the morning" seems like a tired cliché. Nevertheless, for many common physical ailments, low doses of aspirin (acetylsalicylic acid) will make you feel better, and high doses of the drug give sustained relief from the symptoms of chronic inflammatory diseases such as rheumatoid arthritis[1]. Aspirin irreversibly inhibits the cyclooxygenases — enzymes that control the production of prostaglandins (small molecules that induce the pain and fever associated with infection or trauma[2]). However, the difference in the clinical activities of aspirin at low and high doses has led to speculation that not all the benefits of aspirin derive from inhibition of cyclooxygenases. So what might be the target for high doses of the drug? On page 77 of this issue, Yin *et al.*[3] report that high concentrations of aspirin inhibit the recently discovered enzyme IκB kinase-β (IKK-β), and they propose that this effect partially explains the clinical efficacy of high-dose aspirin.

The IKK enzymes (α and β) catalyse the transfer of phosphate moieties from ATP to IκB (reviewed in ref. 4). Phosphorylation leads to the degradation of IκB and release of NF-κB, a transcription factor that is inhibited by IκB. On release, NF-κB rapidly moves to the nucleus where it binds specific DNA sequences, promoting the transcription of genes that influence defence mechanisms such as inflammatory and immune responses. Thus, if IKK-β is inhibited by aspirin, nuclear localization of NF-κB and subsequent transcription should be blocked. This has, in fact, been observed with high concentrations of aspirin[5].

Yin *et al.*[3] now report that high concentrations of aspirin (IC_{50} approximately 50 μM) are required to inhibit IKK-β. They also show that several other kinases, including the homologous and functionally related IKK-α, are not affected by aspirin. Can inhibition of IKK-β and cyclooxygenases explain all the pharmacological effects of aspirin? Let's hope not. The problem with using high doses of aspirin is that it has virtually no therapeutic window — that is, the dose at which aspirin gives relief from chronic rheumatic disease is very close to the dose that generates side-effects, including headaches, dizziness and tinnitus[6]. But, based on the work of Yin and colleagues, we can develop a hypothesis wherein IKK-β is only one of several targets for high-dose aspirin, the unwanted side-effects resulting from activity against other targets.

The anti-inflammatory efficacy of aspirin may, therefore, be limited by two separable factors. First, aspirin weakly inhibits the therapeutic target (IKK-β). Second, it is a similarly weak inhibitor of other, as-yet-unidentified targets, yielding various toxicities. There are many reports of aspirin affecting a variety of biological systems that could be independent of IKK-β inhibition. Most interesting in light of the paper by Yin *et al.* are reports that high concentrations of aspirin inhibit the activation of the Jun-N-terminal kinases (JNKs)[7]. The JNK family of protein kinases mediates phosphorylation of the transcription factor c-Jun, stimulating its ability to promote transcription[8]. Because there is no evidence that IKK-β is involved in activating JNK, these results imply that at least one other target of high-dose aspirin exists.

Although there is a broad consensus that aspirin relieves many of the symptoms asso-