plasmacytomas and Burkitt's lymphoma[11]. The authors therefore investigated the relationship between MYC and IRF4 expression. They find that, in myeloma cells, these two proteins mutually reinforce each other's expression. IRF4 seems to be a master regulator, as its direct targets — many of which are also MYC targets — include mediators of metabolic control, membrane biogenesis, cell cycle, cell death, regulation of transcription, plasma-cell differentiation, glucose metabolism and the production of the cell's energy molecule ATP. It is therefore plausible that, on IRF4 depletion, 'metabolic collapse' also contributes to myeloma-cell death.

As myeloma is a slow-growing tumour, it has been proposed[12] that myeloma cells are differentiated descendants of transformed B cells, which would be the myeloma progenitor cells. IRF4 is inactive in B cells, and IRF4-targeted shRNA does not kill these cells. So treatment of myeloma with IRF4 shRNA, which will kill the shRNA-sensitive plasma cells, should supposedly reveal those rare cancerous myeloma progenitors that are resistant to IRF4 shRNA. But despite extensive investigations, Schaffer *et al.* did not observe such a phenomenon. This suggests that if a 'myeloma stem cell' does exist, it must reside at a stage in B-cell differentiation that requires IRF4.

Despite remarkable improvements in the outcome of myeloma treatment over the past decade, cures are elusive and the clinical management of this cancer remains challenging[13]. The non-uniform and disseminated nature of myeloma, and an inherent and acquired drug resistance resulting from interactions of tumour cells with the bone-marrow microenvironment[14], worsens the prospect of finding new treatments. So the fact that a non-oncogene might be a new therapeutic target for nearly all forms of myeloma is a welcome advance (Fig. 1c). But before contemplating whether Shaffer and colleagues' observations can be translated into the clinic, we must consider whether these data themselves have one or two weaknesses.

The authors performed their studies in myeloma cell lines. All myeloma cell lines exhibit genetic features of highly aggressive disease, which are observed in only 15–20% of newly diagnosed myelomas[7]. Moreover, patients with such molecularly defined high-risk features are not benefiting from current treatments. So, although the finding that depleting IRF4 can kill cells with high-risk genetic features is exciting, one wonders whether IRF4 depletion has lethal effects only in the presence of these high-risk genetic features.

Similarly, the multiple myeloma subtype known as hyperdiploid disease, which makes up nearly 50% of primary myeloma cases, is not represented in the myeloma cell lines Shaffer *et al.* studied. It is therefore unknown whether IRF4 depletion will have similar effects on this and othermyeloma subtypes. The use of cell lines leaves yet another question open: can the bone-marrow microenvironment overcome the lethal effects of IRF4 loss on myeloma cells?

With Schaffer *et al.* testing only about 10% of human genes in their RNAi screen, is it possible that other genes exist that might be more amenable to therapeutic manipulation and whose depletion will have an effect similar to IRF4 loss? Cancer cells are notorious for developing resistance to chemotherapy; will the same hold true for the effect of shRNAs on IRF4?

The authors[4] took advantage of extensive genome-wide expression-profiling data of primary myeloma disease[7,11]. This publicly available myeloma gene-expression atlas[15] provides a comprehensive genomic landscape of the cancer relative to a normal genome. Myeloma cells express about a third of their entire genome. An RNAi library designed to specifically target genes expressed only in myeloma might be a useful step in investigating their individual contribution to cancer and their potential as therapeutic targets. It would be equally important to take the converse approach and screen tumours for the lethal effects of introducing genes whose expression is lost in myeloma cells.

With patient-specific, tailored therapies as a central goal in the post-genomic era, is it possible that more effective shRNAs or drugs emerging from them — easier to deliver and less likely to have adverse side effects — will be identified that target specific genes affected in particular subtypes of multiple myeloma? But perhaps the most crucial question of all is whether non-oncogene addictions are found in other cancer types, especially tumours of epithelial origin, which represent the bulk of human cancers. ■

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ASTEROIDS

How to make a flying saucer

William F. Bottke

Wherever we look in the Solar System, small bodies often seem to come in twos. Simulations show how asteroids spun in the Sun can produce such pairings — one of whose members acquires a strangely familiar shape.

When I was a kid, I used to stay up on weekends to watch the late-night monster movies on television. As I recall, a fair number of these films involved little green men (or women) arriving in flying saucers. The latest news from the Solar System's recesses (Walsh *et al.*[1], page 188) is that our martian neighbours might have had a little local inspiration in choosing the shape of their craft. It seems that thermal forces cause some asteroids to spin up, change shape and shed mass, and eventually evolve into binary systems with a flying-saucer-shaped primary body.

How does this saucer production line work? The answer is that it is solar powered: the torques that modify the spin rates and pole directions of small asteroids are largely created by sunlight reflected and re-emitted from an asteroid at thermal infrared wavelengths. This is the Yarkovsky–O'Keefe–Radzievskii–Paddack (YORP) effect — a mouthful coined by the geodynamicist David Rubincam in honour of four pioneers of the field[2,3]. It can slow down the spinning of an asteroid enough that it falls into a chaotic (tumbling) rotation state, or alternatively spin it up so much that it starts to cast off material from its surface[3].

Walsh *et al.* now report a new addition to YORP's repertoire of outcomes: for kilometre-sized rubble-pile asteroids, their numerical simulations show that the YORP effect can knead the object so that its constituent boulders slide or roll over one another, moving from the poles towards the equator. Over time, this mass movement creates an oblate (slightly squashed) spinning-top-shaped object (Fig. 1, overleaf). This body ends up with bald spots at its poles, where underlying bedrock might be seen if it exists, and a conspicuously fat equatorial belt from which fragments can escape into nearly circular orbits. The high likelihood that these flying saucers have freshly exposed surfaces would make them intriguing targets for our own spacecraft missions.

The authors' simulations further show that fragments ejected from these objects mostly end up accumulating into a single satellite that grows over time. This satellite evolves in

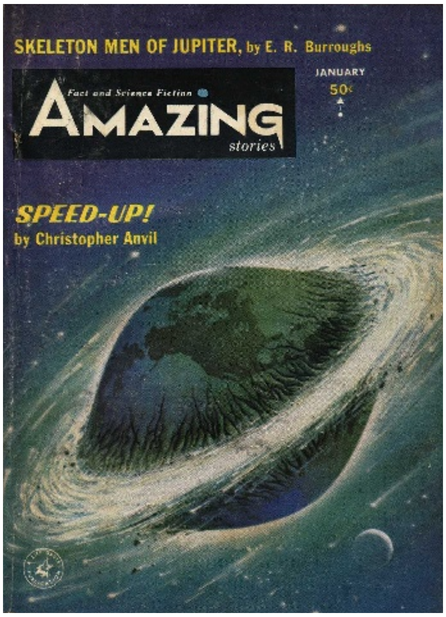

Figure 1 | Science fact. **The spinning-up of celestial bodies by various mechanisms to make flying-saucer-shaped objects, identified by Walsh *et al.*[1] in the progenitors of some binary asteroids, has amazing precedents in the literature. This artwork, by Alex Schomburg, comes from the cover of *Amazing Stories*, January 1964 (Ziff-Davis Publishing).**

response to the accretion of additional fragments, sunlight-driven, non-gravitational forces, impacts, gravitational kicks from its progenitor and — in the case of 'near-Earth' asteroids whose orbits are close to, or even intersect, our own — from close encounters with planets. These mechanisms can also lead to a primary body losing a satellite, but through the YORP effect it readily produces new offspring as long as it has a sufficient reservoir of seed fragments.

A test of Walsh and colleagues' model[1] is its ability to reproduce the features of the radar-observed binary near-Earth asteroid (NEA) 1999 KY36 (refs 4, 5). The primary body of this binary is a top-shaped asteroid of diameter 1.5 kilometres, with an equatorial belt and a period of rotation — 2.8 hours — that is slightly outside the mass-shedding regime. Its bulk density of just 2 grams per cubic centimetre, estimated by precisely measuring the orbit of the binary and thus its gravitation, indicates that, when compared with meteorite data, the object is 50% porous. This is consistent with its being an 'unconsolidated' body made up of loosely packed solid material. The secondary body, with a diameter of 0.5 km, resides on a nearly circular, nearly equatorial orbit 1.5 km from the surface of the primary. Observations of asteroids show that these kinds of diameter ratio, spin rate and orbital distance are common not only among NEA binaries, but also among small-body binaries in the inner 'main belt' of asteroids that lies between Mars and Jupiter[6].

This is not to say that YORP is the only mechanism creating binary asteroids: they can also arise through impacts, and NEA binaries in particular can originate in the splitting of rubble-pile asteroids into gravitationally bound fragments during a close encounter with a planet[7,8]. Whereas such 'tidal' disruption seems considerably less efficient at making NEA binaries than YORP is, impacts might be a more competitive mechanism. Numerical simulations indicate that large asteroid disruptions produce numerous 'escaping ejecta binaries' — fragments launched from the collision site that have similar enough trajectories that they become gravitationally bound together[8]. Such binaries, moving out of the main belt and into the NEA population, would look very different from the flying-saucer binaries.

The armada of flying saucers has outliers elsewhere in the Solar System. Pan and Atlas, two small satellites embedded within the rings of Saturn, also have prominent equatorial ridges, produced by ring particles that struck and piled up on their surfaces[9]. But the mother ship of all of the flying saucers has to be Iapetus. This 740-km-diameter, walnut-shaped moon of Saturn has a protruding waistline, squashed poles, and a discontinuous equatorial ridge that is 18 km high, 200 km wide and 1,600 km long[10,11]. The oblate shape and prominent ridge of Iapetus are reminiscent of features on the smaller flying saucers, and their formation mechanisms might share similarities as well — produced perhaps by a fast spin early in Iapetus' history[11] and/or collisional accretion of particles within a localized disk around the moon[12].

Flying saucers are not the alpha and omega of asteroid shapes and sizes. Since the groundbreaking discovery of a main-belt asteroid with its own satellite (Ida and its moon Dactyl), ground- and space-based searches using state-of-the-art observational techniques have turned up satellite systems in every population of small bodies that we know of — from main-belt asteroids to near-Earth asteroids to Trojans (asteroids that share Jupiter's orbit) to the bodies of the Kuiper belt beyond Neptune[7]. By understanding these populations, what they are like, and how they formed, we can glean insights into the evolutionary history of small bodies throughout the Solar System — although I suspect we are fated never to find one actually carrying those little green men. ■

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SOLID-STATE CHEMISTRY

New order for lithium bromide

David C. Johnson

It's all very well predicting which forms of crystal an inorganic solid can adopt, but how can proof be obtained if these structures aren't thermodynamically stable? The answer is to build them up atom by atom.

Some might say that organic chemists have it easy. When they run a reaction, they can be reasonably confident that the product will be the one they predicted. And if the reaction doesn't proceed as expected, then at least the products will usually be structurally related to the starting materials. Solid-state chemists have no such luxury — the prediction of the atomic arrangements adopted by inorganic structures is more challenging because of the wide variation in structural motifs and geometries that can be adopted by combinations of inorganic atoms[1]. But this looks set to change. Having devised computational methods to predict the atomic configurations of metastable solids[2], Jansen and colleagues[3] now report in *Angewandte Chemie* the preparation of a metastable form of lithium bromide (LiBr), in a process that avoids the formation of thermodynamically stable arrangements.

Quite apart from the difficulties in predicting the extended (lattice) structures of solid-state compounds, practical challenges mark out this field from that of molecular synthesis. When making a molecule, reactions are typically performed in solution, where high diffusion rates allow the reactant molecules to move around and encounter each other readily. The rate-limiting step in these reactions is typically the breaking of a specific chemical bond (which can be tuned by the proper choice of a catalyst), and a dynamic chemical equilibrium exists between the reactants and products. By contrast, the synthesis of solid-state structures typically involves