Hamilton's simple equations allow predictions of expected sex ratios (Fig. 1).

Two additions must be mentioned to account for wrinkles in the *Plasmodium* life cycle. First, the sex ratio of several *Plasmodium* species is female-biased early in the infection, but shifts towards more males as the infection ages[5,6]. When the host mounts an immune attack against the parasite, carry-over of antibodies in the blood meal will kill many male gametes. Male fecundity will decline and more male gametocytes should be produced. Second, low-density infections may result in few gametocytes being transmitted, so male gametes cannot find a female. 'Fertility insurance' would then drive the production of more males[10].

The Reece group[1] used well-characterized clones of *Plasmodium chabaudi* originally isolated from the natural host, African thicket rats (*Thamnomys*), and then inoculated into laboratory mice to initiate experimental infections. Real-time application of the polymerase chain reaction allowed quantification of specific genetic strains and precise measurement of sex ratio.

The authors found that single-clone infections were female-biased early on, but that over time the sex ratio shifted towards males. Single-clone infections should yield 11% male gametocytes early in an infection if **f** = 8 as per malariology lore. Four of the clones behaved according to theory. The two others produced more males, so we can predict the fecundity of these as 1 (the clone designated DK) and 4 (CR) (Fig. 1). Mixing all six clones should give 42% males, and this is just what was observed for the first six days of the infections. This outcome could be spurious if the DK clone dominates in infections (with its high male production), but this clone is known to be a poor competitor and to have low density in mixed infections. Mixing clones two-by-two, the expected result is 25% males, if both clones are equally abundant. But only one clone behaved as expected, with the others producing too few males.

However, Reece *et al.* determined the relative abundance of each clone, finding a negative correlation between the proportion of each parasite clone and its proportion of male gametocytes; when a clone predominated, it was more likely to self, and so produced fewer male cells. Finally, infections with a low density of gametocytes produced more males, even when only a single clone was present, which matches the expectations of fertility insurance.

These results should give cheer to fans of sex-ratio theory because the theory applies even for protist parasites dwelling within blood cells. Hamilton's equations are so simple, yet work so well. This is the real wonder of Reece and colleagues' study; it is as though this 'simple' parasite knows a little algebra.

Further questions have arisen, of course. There seems to be genetic variation for male fecundity (among isolates); why should this be? How does the parasite recognize its own density in the host, and — even more vexing — how does it monitor the presence of kin versus non-kin in other blood cells? Finally, Reece and colleagues' experiments are a study in evolutionary ecology, but in this case the parasite and host have not coevolved, and the ecology is foreign. When a parasite of thicket rats enters a lab mouse, it meets a strange environment. Yet the protist follows the rules laid down in sex-ratio theory. Getting the gametocyte sex ratio right seems to be crucial for *Plasmodium*, no matter what host it visits. Once again, when dealing with sex, it seems that getting it right is all-important. ■

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MATHEMATICAL PHYSICS

# Packings close and loose

Francesco Zamponi

**What determines how grains such as sand pack together to fill a space? A thoroughgoing investigation of how geometry and friction interact in such systems is a step towards a more general understanding.**

How should we arrange objects to pack them as tightly as possible, making best use of all the available space? Packing problems have long fascinated both physicists and mathematicians, but have proved surprisingly tough nuts to crack. Take the 'Kepler conjecture', for instance. It was in 1611 that Johannes Kepler first suggested that the densest packing of identical spheres is achieved by cubic (face-centred cubic) and hexagonal arrangements, with a packing fraction of 74%. Carl Friedrich Gauss produced the first partial proof of this in 1831. What might be a final proof was published only in 1998. It is a 'proof by exhaustion', reached using modern computing power to crunch wearisomely through an inordinate number of possible packing configurations — and its ultimate veracity is still being checked.

Sphere packings are extremely important, not only in condensed-matter physics[1], where they describe the favoured configurations adopted by crystals, but also in computer science and mathematics[2], where they pop up in problems related to group theory, number theory and error-correcting codes. On page 629 of this issue, Song, Wang and Makse[3] take a significant stride towards a unified theory of a particular type of packing — not of the regular packings of the Kepler conjecture, but the random, amorphous packings that model the behaviour of everyday granular materials such as sand and nuts (Fig. 1).

When spherical grains are randomly thrown into a box and shaken, they form an amorphous arrangement with a packing fraction of 64%, significantly lower than the 74% of the densest possible crystalline packing. Remarkably, this final density — the signature of 'random close packing' — was found to occur however the samples were prepared: whether by throwing grains into a box, shaking them and allowing them to settle; depositing them randomly around a disordered 'seed cluster'; slowly compressing a looser arrangement; and so on.

If small regions of regular, crystalline packing are created first, a random close packing can then be continuously compacted until a denser, entirely crystalline structure is obtained[4]. When looking at individual configurations, therefore, the density value 64% does not seem to have any special importance. Its relevance must instead be related to the statistical properties of an ensemble of packings produced by a given method. Is random close packing favoured for entropic reasons, such that there are just many more ways of jumbling grains up to form a random close packing than any other configuration? Is it a well-defined 'metastable' state that can persist for a considerable time? Or is it related to a hidden critical point, such that particularly large numbers of particles must be rearranged to change the density (a quality characterized by a large 'correlation length')? Many attempts have been made to achieve the statistical description of random close packings that such questions demand[5–9]. These studies, supported by numerical simulations, revealed how important geometry, and in particular the network of particle contacts[5], was in determining the density and other structural features of the final packing.

Random loose packings are related to

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**Figure 1 | Balls from regular to random.** Johannes Kepler investigated the highest packing density of regular arrangements of spheres — here illustrated (left) by a face-centred-cubic stacking of golf balls. Less regular packings (right) are the subject of Song and colleagues' investigations[3].

random close packings, but are even more elusive. They are obtained by letting spheres settle very gently[10]; the loosest stable packings that have been achieved have a packing fraction of about 55%, and friction is known to determine their stability. Is there a consistent statistical theory that can account for both close and loose random packings? Are the close and loose packings special points, or do similar stable configurations with packing fractions between 55% and 64% exist? Do these packings have critical properties such as a large correlation length[5,11]? What is the relative importance of geometry and friction?

Song *et al.*[3] provide answers to some of these questions. They develop a consistent, although approximate, mean-field theory of 'jammed' amorphous packings. A mean-field approach works by modelling the average interaction between bodies, thus making it the same for all the bodies in the packing. It is usually the first step towards any more sophisticated computation. The authors start by deriving a relation between the unoccupied space in any locality and the local geometrical coordination, which is defined as the average number of contacts per particle. The mean-field assumption means that some of the niceties of particle correlations are neglected, but the result agrees well with experimental data[12]. The derived relation indicates that the packing fraction, which is directly related to the free volume, is determined solely by the geometrical coordination.

The authors go on to show that not all geometrical contacts carry a non-zero force. As a consequence, they introduce a mechanical coordination number, defined as the average number of contacts carrying a non-zero force. On the basis of numerical simulations, they assume that this number is a universal function of the friction coefficient, and is independent of the way the sample is prepared.

The emerging picture is thus of mechanical coordination determined uniquely by friction, and geometrical coordination related to density. Considerations of general stability require that both coordination numbers are somewhere between 4 and 6 (the mechanical coordination number is by definition smaller than the geometrical coordination number). One then finds a collection of states satisfying these bounds, and draws a phase diagram by plotting two independent variables chosen from among the density, friction and the two coordination numbers of the states against each other. Song *et al.*[3] choose density and mechanical coordination number. The final prediction is that if, for instance, friction is fixed (as it is in experiments), one can obtain packings with a whole range of densities (Fig. 2). The authors thus rationalize what is suggested by many experiments from the perspective of statistical mechanics.

An intriguing question immediately raised is how one might predict in which precise state a given preparation procedure will end. The authors follow a 20-year-old suggestion[13] in introducing a variable they term compactivity. Compactivity is akin to an inverse pressure, in that it decreases as density increases, and Song *et al.* produce some numerical evidence that, like thermodynamical pressure, it could be a 'state variable' that links different, seemingly independent, experimental control parameters.

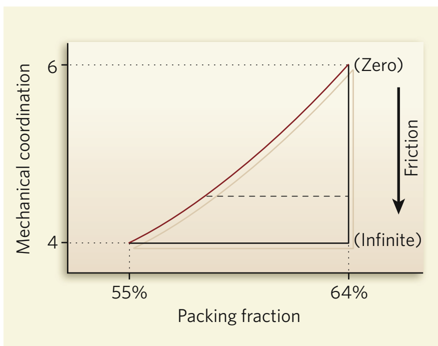


**Figure 2 | Phases of packing.** In Song and colleagues' phase diagram[3], for a given friction (which determines the mechanical coordination) a range of possible densities exists (dashed line) — except at zero friction, where the density of random close packing, 64%, is a unique point. (The higher the mechanical coordination number, the lower the friction: friction blocks sliding modes and so fewer contacts are needed in order to make the packing stable.) Note that the geometrical coordination number for a given density is the maximum value of the mechanical coordination number. The 64% packing fraction of the random close packing corresponds to a geometric coordination number of 6; 55% (random loose packing) has a geometric coordination number of 4.

Similar ideas have emerged in related contexts, such as the physics of glasses and problems of combinatorial optimization[8,14]. In the latter example, researchers have tried to find a relationship between the behaviour of algorithms searching for solutions and the presence of transitions between different phases, and to identify state variables that could characterize these phases. Results so far have been contradictory, with some of them bringing into question the validity of this idea in situations beyond simple mean-field models[15]. But the perspective offered by work such as this, and that of Song *et al.*[3] — with its promise of transforming complex problems of non-equilibrium dynamics into much simpler statistical problems — is too fascinating to abandon, and the wait for new results will not be long. ■

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