

PERSPECTIVES

Wnt, a large majority (~80%) of the clones were very small and only formed sensory neurons. This result implies that Wnts do not affect proliferation of multipotent neural crest progenitors, but rather bias their fate toward a sensory phenotype. In a complementary experiment, this same group found that loss of Wnt signaling in neural crest cells causes loss of both the sensory and melanocyte lineages (10). Taken together, these data suggest that Wnt signaling acts early in the neural tube to promote sensory fate decisions in multipotent neural crest progenitor cells.

The new work nicely shows that the Wnt pathway promotes sensory neurogenesis. But how do we reconcile this with other studies where activation of Wnt signaling drives neural crest cells to form melanocytes in the zebrafish or causes overgrowth of the

dorsal neural tube in the mouse? The issue is very likely to be one of timing. Perhaps activation of Wnt signaling in early neural crest progenitors promotes a sensory fate, whereas later activation promotes pigment cell differentiation. This difference in timing could explain the differences in the gain-of-function (2) and loss-of-function (10) phenotypes. There is ample evidence that Wnts play multiple roles at multiple times, even in the same cell type. The challenge in the future will be to understand how the same ligand can elicit such different responses depending on the stage of development. In addition to stimulatory factors, migrating neural crest cells encounter environments rich in inhibitors that may counteract the influences of signaling molecules such as Wnts and BMPs. Perhaps these inhibitors titrate or delay responses as neural crest cells migrate

along particular pathways. In this way, the lineage choices of neural crest progenitor cells may become progressively more limited as development proceeds.

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PHYSICS

Packing in the Spheres

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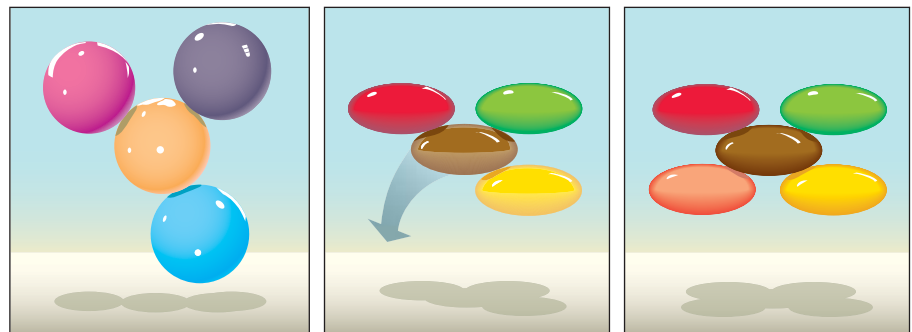
How many candies are in the bag you had for a snack with your coffee? How many grains of sugar are in the package you added to your coffee? And how many coffee beans came in the package that you used to brew the java? These may seem like idle questions, but they are, in fact, very important. The answers tell us how to pack materials efficiently, taking up the least volume possible, and are thus of critical interest to merchants, packagers, and shippers. Physicists, materials scientists, and mathematicians have also been studying these questions for centuries, and in recent years, it has seemed that the solution to these questions was becoming clear (1–3). Physicists have traditionally cast the problem in terms of that simplest approximation to all objects, the sphere. However, as reported by Donev *et al.* on page 990 in this issue (4), the behavior of spheres is apparently the exception rather than the rule. As soon as the shape of objects becomes nonspherical, the packing efficiency increases by a surprisingly large amount.

The question of packing at first seems very simple: How many marbles can you pack in a jar? To keep things simple, of course, you use perfectly spherical marbles, and to quantify the answer, you will measure the volume fraction, ϕ , occupied by the marbles. A simple experiment to do, but one that

is tricky to understand. If you put the marbles in the jar very gently, a relatively small number will fit, with a volume fraction of around $\phi \approx 0.6$. But then, if you very gently shake the marbles, so that they pack down as much as possible, but still remain completely disordered, their volume fraction increases to about $\phi \approx 0.64$. This is the highest volume fraction of spheres packed to retain a random configuration, and is called random close packing, or ϕ_{RCP} . Virtually all the spheres are jammed in place, so none can move. Indeed, extensive experimental studies (3) of random packings give this value for the maximum volume fraction. Similarly, computer simulations (5, 6) with several different algorithms give the same value. Thus, it has long been thought to be a universal value, even though its actual magnitude cannot be predicted analytically.

There are two other important ways that our jar of marbles can be packed, however. The first occurs if you shake the jar very hard, allowing the marbles to jump up slightly and completely rearrange themselves. Then they begin to order, forming layers of spheres packed in a hexagonal lattice, with each layer nestled in the hollows formed by the layer beneath it. This structure is nearly crystalline, and forms the highest volume fraction packing of spheres, with $\phi = 0.74$. Interestingly, although we are intuitively sure that this is the highest volume fraction packing of spheres, it has only been rigorously proven in the past few years (7).

The second important form of packing occurs if you pack the marbles even more gently than for random close packing; in fact, you must first put them in a fluid that provides neutral buoyancy, so there is no gravitational force whatsoever. Then, after the marbles settle, the packing seems even less dense and the volume fraction is only $\phi \approx 0.56$ (8). This is called random loose packing, and represents the minimum pack-



Shape is destiny. The shape of objects has a big effect on how densely they can be packed into a given volume. (Left) Spherical objects can only be pushed sideways and not rotated by neighbors, so they cannot experience torque. (Middle) Ellipsoidal objects can be rotated away by their neighbors and escape confinement. (Right) As a result, more neighbors (and denser packing) are required to balance the forces on an individual ellipsoid than on a sphere.

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ing of spheres that still keeps the particles jammed in place. However, this form of packing is somewhat controversial (6, 9). Is this a meaningful number, or is it a function of exactly how the particles were arranged?

Although the question of packing of spheres has been of vital interest and importance, most real objects that we want to pack are not spheres, but are more irregular in shape. However, it has long been assumed, as physicists are wont to do, that what happens for spheres is immediately applicable to more complex shapes. It is, therefore, a great surprise that this is not the case at all. The new results are based on a very important question: If you use M&M's (a most ubiquitous object in some corners of the Princeton Physics Department where this work was done), how many candies can you pack into a large barrel? The result found by Donev *et al.* is surprising: The maximum volume fraction, while still keeping the candies completely disordered, is closer to $\phi \approx 0.72$, much larger than it is for spheres. There are many more candies in that barrel than you thought.

Donev *et al.* do indeed use M&M candies, but of course, only the plain chocolate variety. They show that M&M's are nearly perfectly monodisperse ellipsoids. Repeated experiments, with different-sized ellipsoidal M&M's, give the same large number for the volume fraction. These experiments inspired a careful numerical investigation,

in which the shape of the ellipsoids is systematically varied. The results suggest that, in fact, the more general value for the largest packing of irregular objects is actually about $\phi \approx 0.74$. Spheres actually seem to be an anomaly, with the maximum volume fraction for random close packing dropping surprisingly sharply as the shape approaches that of a sphere.

The reason for this anomaly is not yet fully understood, but may well go back to the case of the still-disputed random loose packing. It has to do with the fact that the particles must be jammed in place, and must be in what is called static equilibrium (see the figure). That is, each particle has several nearest neighbors that touch it, and therefore exert a force on it. However, because each particle is perfectly stationary, or jammed in place, the sum of all the forces on it must be identically zero. Thus, there must be no net force to cause the particle to move, and no net torque to cause the particle to rotate. For a perfectly symmetric object, such as a sphere, the forces exerted by the neighboring particles can only cause it to translate; they cannot cause it to rotate; thus there can be no torque on a sphere. By contrast, for an ellipsoid, the forces exerted by the neighbors can cause both a translation and a rotation. As a result, to ensure that all the forces sum to zero for an arbitrary orientation of neighbors, several more neighbors are required, on average, for the ellip-

soidal M&M's than for the spherical marbles. This in turn requires the higher volume fraction observed.

This higher volume fraction has many important consequences. It explains how to pack objects into a smaller volume, which is important for storage and shipping. The key is to ensure that the particles are not spherical. It also suggests ways to achieve a higher volume fraction of particles for making things such as building structures or ceramics. However, perhaps most important, it explains why eating M&M's for lunch one by one always takes longer than eating a bag of spherical candies of the same total volume. This is, of course, crucial information when you are dieting and M&M's are the only food you eat all day.

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NEUROSCIENCE

Conflict and Cognitive Control

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Cognitive control is necessary when we block a habitual behavior and instead execute a less-familiar behavior. Because cognitive control requires an effort, it is not efficient to maintain a high level of control all the time—the nervous system needs to know when cognitive control is necessary. On page 1023 of this issue, Kerns *et al.* (1) investigate the brain mechanisms that underlie the recruitment of cognitive control.

Two cortical areas in the frontal part of the brain, the anterior cingulate cortex (ACC) and the lateral prefrontal cortex (LPFC), are considered essential for recruiting cognitive control. This conclusion is based both on the psychological examina-

tion of brain-damaged patients and on the imaging of normal human subjects (2). Botvinick and colleagues have proposed that the ACC detects conflicts between plans of action, and in response to these conflicts recruits greater cognitive control in the LPFC (3). This hypothesis is consistent with evidence showing the involvement of the LPFC in the execution of cognitive control, such as selective attention and response inhibition (4). Activation of the ACC by action-plan conflicts has also been reported (5–7). However, as yet there is no direct evidence of a connection between the detection of conflicts in the ACC and the subsequent greater control recruited in the LPFC.

The Stroop test is a useful tool for examining this connection. In this test, words denoting colors (such as red or green) are presented to human subjects in a variety of different colors, one at a time. The subject is instructed to report the physical color in which the word is presented (the color-

naming condition) or the color that the word denotes (the word-reading condition). Subjects find it difficult to respond correctly in the color-naming condition when the physical color of the presented word is different from its meaning (incongruent). This difficulty is apparent not only in the subject's frequency of erroneous responses but also in the subject's reaction time for correct responses. The reaction time tends to be longer in incongruent trials than in congruent trials (where the physical color matches the meaning). Because human subjects are well trained to read words, a motor plan for reading the presented word is spontaneously initiated, contrary to the instruction to report the color in which the word is presented. This results in a conflict between two plans of response actions, which in turn increases the reaction time (see the figure, left). Functional magnetic resonance imaging (fMRI) has revealed greater activation in the ACC during incongruent versus congruent trials (6).

When an incongruent trial is followed by another incongruent trial, it is expected that a conflict detected in the first trial recruits greater cognitive control in the second trial. Thus, there should be stronger

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